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ORIGINAL ARTICLES

THE METABOLISM OF BILIRUBIN

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INTRODUCTION

By EDWARDS A. PARK, M.D.

A little girl was asked by her teacher to write an essay on Benjamin Franklin and to make it short. She wrote: "Benjamin Franklin was born in Boston: he married a Philadelphia lady and discovered electricity." Dr. Najjar made an independent discovery of electricity in Missouri, a gentle, even and altogether pleasing current. I shall be short in my turn.

I regard my function on this occasion to be like that of a keeper whose business it is to exhibit to you a greyhound and, after demonstrating his points and recounting his exploits, to turn him loose.

Victor Najjar was born in Lebanon. He graduated from the American University of Beirut in 1932. After interning in pediatrics at the American University Hospital, Beirut, 1935 to 1937, he became instructor in Public Health and Hygiene at The Rural College for Teachers, Bagdad, Iraq, and the following year pediatrician-in-charge to the Children's Clinic, Bagdad. Najjar's residence in Bagdad leads me to believe that he could tell us much about grand viziers, caliphs and harems. In 1939 he came to this country joining the pediatric staff of Johns Hopkins University. In 1944 he became Associate and in 1945 was promoted to be an Assistant Professor of Pediatrics. In 1946 he was accorded a National Research Council Fellowship and elected to the laboratory of Carl F. Cori, Washington University School of Medicine, St. Louis, where he remained until

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1948. His work there was so outstanding that, an exception being made, his fellowship was extended for the third year so that he might obtain additional experience in the laboratory of Ernest F. Gale, School of Biochemistry, University of Cambridge, England, in the enzyme chemistry of bacteria. On the expiration of his fellowship Najjar returned to the Harriet Lane and was made Associate Professor of Pediatrics at Johns Hopkins University in 1949.

Najjar was a discovery of L. Emmett Holt, Jr., and owes a great debt to him. Indeed, Najjar's contact with Holt was the pivotal point in his career, since it not only gave Najjar his start in this country but it also determined the fruitful direction of his studies into the fertile field of vitamin and enzyme chemistry.

I shall not discuss Najjar's work in detail but rather point to certain peaks rising above the general elevated plateau of his accomplishments. The first highly important work which was done with Holt in collaboration was the discovery of a new metabolite of nicotinamide together with a method for its assay which latter has since had wide usage. The work of Najjar and Holt resulted finally in the recognition that the metabolite was a methylnicotinamide which Perlzweig later characterized more definitely as the N-methylnicotinamide. Based on this finding Najjar developed a test to measure the methylating function of the liver. The next outstanding feat, this time done in Cori's laboratory, was the crystallization of phosphoglucomutase, the so-called second Cori enzyme, which changes glucose 1-phosphate to glucose 6-phosphate, the second step of the glycogen breakdown. Najjar perceived that the inhibition of that enzyme by an inhibitor was due to the formation of a metal-substrate-inhibitor complex. The result of this was the theory, proposed a year ago, now gaining recognition, that the true substrate of most enzymes was a metal-substrate-complex. At the recent symposium on "The Physiological Rôle of Certain Vitamins and Trace Elements" at the McCollum-Pratt Institute in honor of Dr. E. V. McCollum, I heard Dr. William D. McElroy, Director of the Institute, express the opinion that Najjar's conception was probably true. Najjar's latest peak has been the crystallization of bilirubin and the studies of the properties of the direct and indirect types of this pigment, work done in the Harriet Lane. Najjar will discuss this subject presently.

Although all of Najjar's 35 contributions to scientific knowledge have been on biochemical subjects and borne, some of them, rather formidable biochemical titles, it must not be thought that he is not a clinician. Najjar is an able clinician and an unusually facile administrator. We would all of us write on biochemical subjects and be profound if we only knew how. Najjar has a brilliant mind and possesses a world culture, all too rare in this country at the present time.

I now revert to my original figure. I said at the beginning that I regarded Najjar as a particular greyhound and conceived it as my duty to exhibit him to you and then to turn him loose. I now proceed with all the dignity and formality I can muster to release him, taking off his muzzle.

THE chemical nature of the bile pigments and the breakdown of hemoglobin to bile pigments have been under investigation for a very long time.[1,2] Much has been discovered that is of great importance to physiology and to the understanding of disease. Much remains obscure and more information is to be desired.

It seems reasonably certain that bilirubin is the final stage in the breakdown of hemo-

globin in the body. What happens to this pigment after it reaches the gut belongs more to the realm of microbiology, in so far as it is transformed further to urobilin, urobilinogen, etc., by bacterial action. It is therefore of great importance to study the nature of the bile pigments at the bilirubin stage, before it gets to the bowels and prior to its degradation by extraneous factors unrelated to human physiology. This is of particular value when it is realized that there are many heme compounds in the body, other than hemoglobin that might give rise to bilirubin. Myohemoglobin, the cytochrome system, catalases and peroxidases are but a few examples. It is still doubtful whether the heme of myohemoglobin, under physiologic or pathologic conditions of muscle destruction, gives rise to bile pigments and very little is known regarding the fate of the heme of the other heme proteins.

A striking example of the need for a thorough chemical study of native bilirubin in serum has been under investigation in our laboratory during the past year. We were confronted by a new entity which Dr. Crigler and I have termed "congenital familial nonhemolytic jaundice with kernicterus."[3] In this disease the child is born with jaundice that persists. There are also associated signs and symptoms of neurologic involvement and severe mental retardation. The disease is usually fatal. There is a definite familial pattern of heredity pointing to a genetic mutation of the recessive type. There is no blood group incompatibility and no evidence of hemolysis, yet the bilirubin is greatly elevated (10 to 44 mg./100 cc.). The daily output of bile pigment through the liver is normal, as shown by normal urobilin excretion. This accumulation of bilirubin may then be due either to a high threshold requirement by the liver or to an abnormal type of bilirubin. In view of the lack of hemolysis and the associated pathology in the brain, the possibility that the bile pigment originated in the respiratory ferment or other heme enzymes was entertained. This is in harmony with our knowledge that brain is very sensitive even to mild states of anoxia. A state of tissue anoxia would certainly prevail if the cytochrome system is defective. We have not solved this problem, yet only by isolating the pigment were we able to tell that it was not mesobilirubin. This illustrates vividly the necessity for rigid characterization of bile pigments in their native state.

The purpose of this presentation is to discuss the studies Dr. Barton Childs and I made on the chemical nature of bilirubin, the process of isolating these pigments in crystalline form from serum[4] and characterization of their properties.[5]

Since Van den Bergh's[6] recognition of the direct and indirect types of pigment, a great deal of confusion has attended research in this field. In this connection Lemberg and Legge[1] in their recent book state that "there are few fields in biochemistry where so much work has been done with so little success." It was necessary first to settle the question raised by conflicting reports[1] regarding the attachment of the pigments to serum proteins. For this purpose we used fractionation of human sera with ammonium sulfate—sera from children with definite atresia of the bile ducts and from patients with hemolytic jaundice of one type or another. We measured (see chart 1) the bilirubin content of each ammonium sulfate fraction in the Beckman spectrophotometer using the formula for bilirubin absorption (A) at 460 mμ and 420 mμ: True absorption at $460 = A460 - \frac{A420 - (A460 \times 0.86)}{4}$. This corrects for unavoidable contamination of sera with hemoglobin which interferes in the Van den Bergh reaction. We found that, when

fresh sera were used and all manipulations done at 4°C., the direct reacting pigment in sera from obstructive jaundice showed a distribution in the various fractions that closely followed that of serum albumen. On the other hand the indirect reacting pigment from sera of hemolytic jaundice showed a distribution pattern similar to that of the globulin fraction. Thus the distribution maximum of the indirect fell at 0.54 to 0.58 salt concentration and that of the direct at 0.44 to 0.48 concentration. There is little doubt in our minds that in obstructive jaundice the pigment is combined with the albumen and in hemolytic jaundice it is combined with the globulin fraction (chart 1).

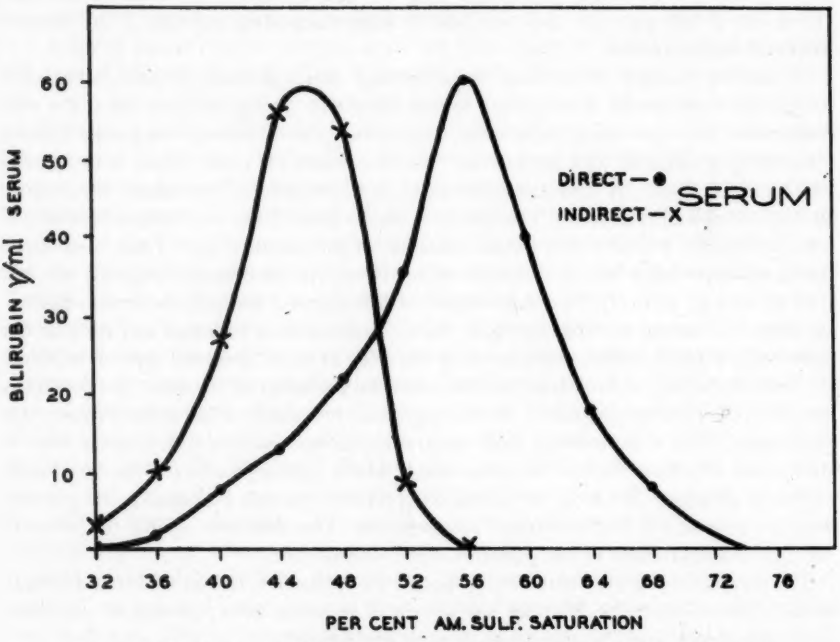

CHART 1. Distribution of bilirubin in different ammonium sulfate fractions of direct (obstructive jaundice) and indirect (hemolytic jaundice) reacting sera.

It became necessary then to ascertain whether the difference in the chemical behavior of these pigments lies in their association with different proteins or whether it is inherent in their chemical or physical constitution. The obvious way to approach this problem is to isolate both pigments free of protein and compare their chemical properties. We were fortunate in devising a simple method whereby the indirect pigment could be readily obtained in crystalline form (Fig. 1).

The method* consists essentially of extracting serum at pH 5.0 with ether, and washing the ether thoroughly with water. The pigment is re-extracted from ether by 0.005-0.01 Molar pyrophosphate buffer pH 9.5, then brought down gradually to pH 7.6 at which point crystals begin to appear and proceed to completion overnight at 4°C. Serum 0.1 to 1.0 cc. can be used and as little as 20 γ of bilirubin can be crystallized with relative ease. All indirect reacting sera from any source behave similarly in that the pigment

crystallizes easily (see table 1). We have obtained crystals of identical appearance from cases with hemolytic jaundice, sickle cell anemia, jaundice of the newborn and jaundice following blood incompatibility. The same type of crystals and with the same relative ease were obtained from subdural hematoma fluid. When this pigment, so obtained, was subjected to coupling with diazo reagent, it behaved as an indirect pigment (Fig. 1).

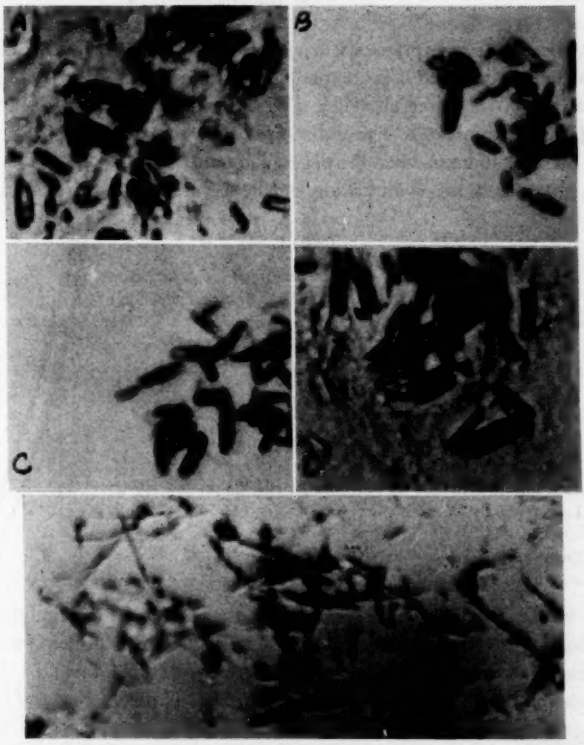

FIG. 1. Indirect bilirubin crystals obtained from sera of cases with (A) hemolytic jaundice, (B) jaundice of newborn, (C) sickle cell anemia with jaundice and (D) from subdural hematoma fluid. (E) Direct bilirubin crystals from obstructive jaundice serum. Crystals from indirect serum are thin plates and those from direct are rods with blunt ends. ×2200.

The problem of the direct pigment was not as simple as this. We can extract it,* purify it and crystallize it using a totally different method. It is, however, necessary for comparison to use the same method as that of the indirect so that no possible modification of the molecule would occur from the use of different reagents. Unfortunately using the method previously outlined the yield was about 2% since the direct pigment is almost insoluble in ether at pH 5.0. Large volumes of ether along with repeated extraction permitted the isolation of enough material to render a few experiments pos-

* The details of the procedure and study of the chemical nature of the direct and indirect bilirubin will be published elsewhere.

sible. We succeeded only once in 20 trials in crystallizing it. All tests were therefore made on the pyrophosphate extract adjusted to the desired pH. This pigment proved again to retain its original characteristic of direct diazotization. Like the parent serum it was more unstable than the indirect when placed under identical conditions of pH and salt concentration. Its instability was manifested at higher pH values (8.0 +) by oxidation to biliverdin and at lower values by transformation into the indirect type of pigment (chart 2).

Having obtained these two pigments in relatively purified form, it became feasible to study other physical and chemical properties. It was found that both had a similar absorption maximum at 440 mμ (see chart 2) with an extinction of 46 to 48 mM in 0.01 M pyrophosphate buffer pH 8.2. The indirect becomes direct by keeping it at pH 10.5, and the direct becomes indirect when the pH is maintained below 7.0.

We have also studied the combination of the pigments with protein at pH 8.2 in

TABLE 1

STEPS USED FOR CRYSTALLIZATION OF INDIRECT BILIRUBIN ALONG WITH RECOVERY VALUES AT EACH STEP

Crystallization of Bilirubin	
Procedure	γ Recovered
pH adjusted to 6.0 with 0.2 M phos. buffer	220
Extraction with ether—wash ether	210
Extraction with 0.01 M pyro. buffer pH 9.5	208
Lower pH to 7.6 with phosphate buffer pH 7.0	—
Cool to 4°C.	—
Overnight crystals	180

pyrophosphate buffer. For that purpose the shift in the absorption maximum from 440 mμ in aqueous solutions to 460 mμ, when bilirubin combines with protein, was utilized to measure the extent of combination. Similar studies were performed by Martin.[7] We found that both combined with a ratio of 2 mol./mol. albumen, that the indirect combined more readily with α globulin and no combination took place with γ globulin or globin.

It appears then that the two pigments are distinctly different in their behavior both when in their native state in serum or when isolated in more or less pure form. There is little doubt, however, that their chemical constitution must be similar insofar as one form can be transformed to the other rather readily and with gentle manipulation. Whatever difference does exist, it is unrelated to the nature of protein combined with the pigment. The transformation of direct to indirect can also be observed in the serum itself. When direct serum is incubated for a few hours at 37°C., the fractionation pattern with ammonium sulfate shows a shift to the pattern of the indirect serum. Furthermore the changed pigment becomes extractable with ether at pH 5.0 and readily crystallizable. This change is not enzymatic. We have not succeeded in obtaining a change in the type of bilirubin by incubating either serum or the pure pigment with liver or kidney homogenates under various conditions of pH and salt concentration.

It seems clear then that the two different types of bilirubin differ slightly. The dif-

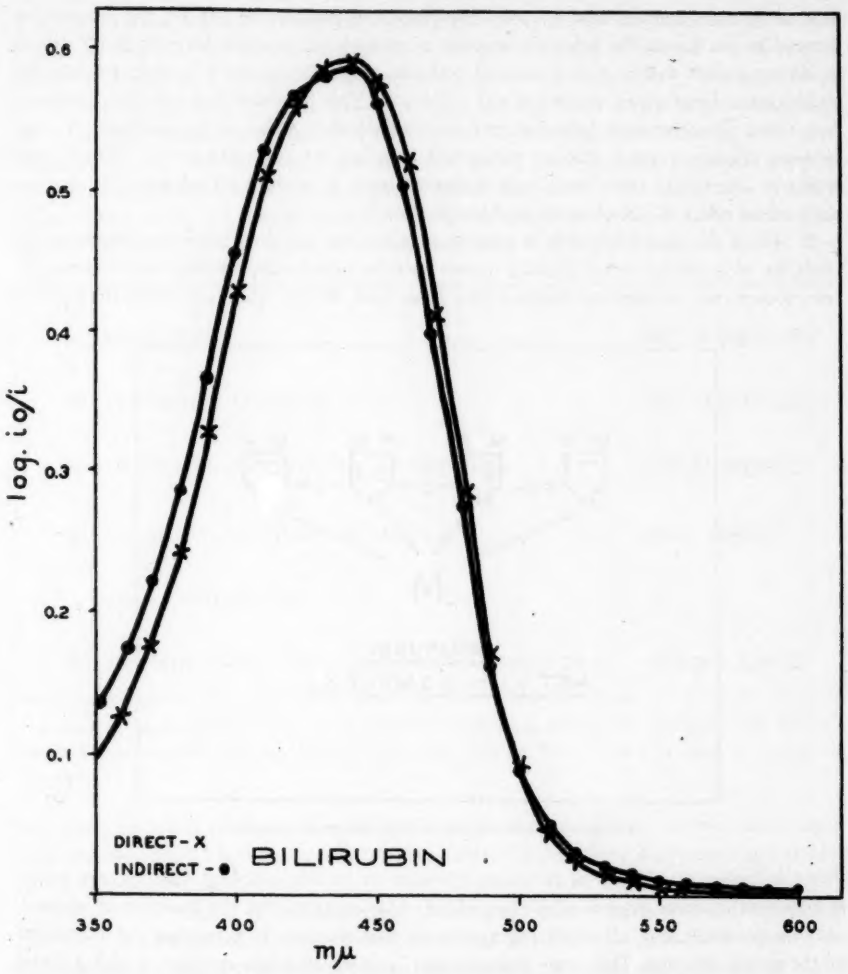

CHART 2. Absorption spectra of direct and indirect bilirubin in 0.01 M. pyrophosphate buffer pH 8.2. Both pigments showing maximum at 440 mμ.

ference is not explicable by an extra radical, conjungation or condensation. Were that the case, the transformation would require cleavage with drastic treatment and probably the liver and kidney tissue would possess the necessary enzymes for that cleavage. Such is not the case and the process seems to be a physico-chemical process.

The first suggestion of the nature of the chemical difference was offered by the following observation. Direct bilirubin, obtained in (0.005M) pyrophosphate extracts pH 10.0 from direct reacting sera, remains in solution when the pH is brought down from 9.5 to 5.0. By contrast indirect bilirubin from indirect sera, treated similarly, begins to precipitate about pH 7.5 and is insoluble at pH 7.0 or below. When, however, indirect bilirubin is ex-

tracted in more concentrated (0.2M) pyrophosphate solution of pH 10, the pigment behaves like the direct. The bilirubin remains in solution and is stable for days at 4°C. There is no suggestion that it is in a state of colloidal suspension since it is quite reactive and maintains a direct diazo reaction at pH 1.8 to 2.5. This indicated that complex formation has taken place between bilirubin and a contaminating metal in the solution. A magnesium, calcium, copper, iron or manganese complex can form (chart 3). This is quite different chemically from metal salt formation such as sodium bilirubinate.[2] It also can explain the effect of pH observed by Cabello-Ruiz.[8]

If indeed the direct bilirubin is a metal complex one can then prevent or break up the complex with strong metal binding agents such as 8-hydroxyquinoline and versene, the tetra sodium salt of ethylene diamine tetra acetic acid. When either is added to the aqueous

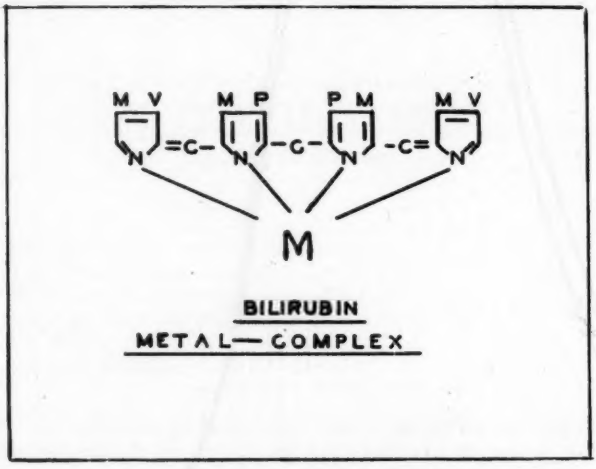

CHART 3. Formulation of bilirubin metal complex.

direct bilirubin at pH 9.5 or to direct bilirubin in serum, coupling fails to take place. It also fails to occur even if alcohol is added. This suggests that the function of alcohol, caffeine or cholic acid, all catalyzing agents for this reaction, is to catalyze the formation of the metal complex. This same phenomenon is observed when cysteine, a strong metal binder, is used for this purpose. When appropriate and equal molar concentrations of cysteine, histidine and glycine at pH 9.5 are added to the direct aqueous or serum bilirubin, the degree of inhibition of the diazo reaction produced depended on the metal binding capability of the amino acid. The inhibition was 100% with cysteine, 65% with histidine and 10% with glycine. This closely parallels the relative metal binding ability of these amino acids. These findings strongly suggest that the diazo reaction is dependent on the formation of a metal-bilirubin complex and that alcohol seems to catalyze the formation of this complex. Accordingly, the direct bilirubin is a bilirubin-metal complex and the indirect bilirubin represents bilirubin not bound to metal. The metal complex is formed at high pH, is unstable at low pH unless the solution is of high ionic strength. It is decomposed by mineral acids and heat. These findings explain why commercial bilirubin obtained from bile is actually indistinguishable from

our crystalline indirect bilirubin since the metal complex is destroyed in the process. It is appropriate then to postulate the following mechanism for the behavior of the bile pigments. Heme is converted to biliverdin by oxidative rupture of the porphyrin ring as shown by Lemberg[9] (see chart 4). Biliverdin is reduced to bilirubin.[10] This is attached to the globulin fraction. The pigment is excreted into the bile where it encounters a high pH with high concentrations of metal ions. Under these optimum conditions, a bilirubin metal complex is formed. When there is obstruction of the bile ducts, the metal complex is forced back into the blood stream. Under those conditions it attaches to the albumen of the blood serum. The attachment to the protein would be expected to be firmer than that of the indirect, since in the metal-complex state it is a more polar molecule. This

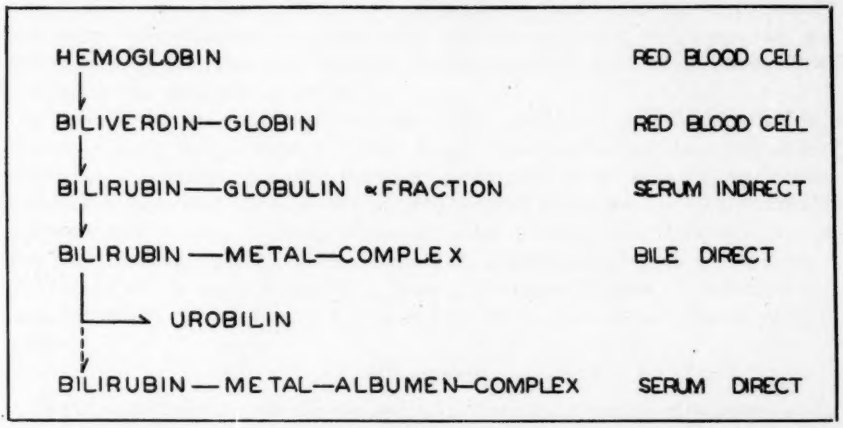

CHART 4. Steps formulated during hemoglobin breakdown to bilirubin. Dotted arrow indicates bilirubin-metal-albumen complex formed when bile re-enters blood stream in cases of biliary obstruction.

is in contrast to the observation made by Coolidge who postulated a firmer combination with the indirect.[11] The ease by which we can extract the indirect is evidence against this and in favor of our view.

Finally, I feel that it is indeed a great pleasure to be honored before a distinguished gathering of this nature. I must confess, however, that I already feel the weight of responsibility that any award imposes upon the recipient. It is the responsibility of maintaining a high quality of performance in order to do justice to you and particularly to those who showed their faith in me and made this occasion possible. I hope I shall not fail.

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The Johns Hopkins Hospital

SUBDURAL HEMATOMA, A COMPLICATION OF OPERATION FOR HYDROCEPHALUS

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AMONG a group of 24 infants undergoing surgical treatment to relieve congenital internal hydrocephalus, the writer has observed three patients in whom subdural hematoma developed during the early postoperative period, following decompressive procedures. Unfortunately, this complication was not recognized in the first case and proved fatal; in the other two, convalescence was prolonged and cerebral damage from compression was no doubt aggravated.

It appears that subdural hematoma should be considered a possible sequel of any procedure which brings about relatively abrupt decompression of the cerebrum. Its occurrence is probably rare when the cerebral ventricles are of approximately normal proportions, but when there is well marked internal hydrocephalus with ventricular dilatation and thinning of brain substance, sudden relief of intracranial hypertension may not uncommonly precipitate bleeding into the subdural space on one or both sides.

Attempts will be made in this paper to point out salient features of mechanism and diagnosis of this complication, and consideration will be given to its treatment and prevention.

MECHANISM

The brain of a patient with chronic internal hydrocephalus exhibits enlargement of the lateral ventricles and thinning of white and gray cerebral substance, due to sustained elevation of intraventricular pressure. These changes are often pronounced, and they may be extreme, with huge ventricles and ironing out of cortex to a thickness of only a few millimeters. In such cases, the cortex maintains its normal convex contour closely apposed but not adherent to the dura mater, by virtue of constant pressure of cerebrospinal fluid within the ventricular system, rather than by inherent strength or rigidity of the brain itself. Some support is given the brain by superior cerebral veins which leave the superomedial margin of each hemisphere at irregularly spaced intervals, pass through the subdural space between arachnoid and dura, and enter the superior sagittal sinus. Similar relationships obtain along the inferolateral border of the temporal and occipital lobes, where veins proceed into the lateral sinus.

When intraventricular pressure is reduced by withdrawal of cerebrospinal fluid, support of the thinned-out cerebral substance is diminished and the brain tends to collapse, falling away from the dura and widening the subdural space, often to marked degree, depending upon volume of fluid evacuated as well as rate and duration of such withdrawal. Frequent coexistence of abnormal skull enlargement amplifies this process, causing greater discrepancy in volume between cranial cavity and cerebrum. As the brain sags, traction is brought to bear upon the supporting veins, and this force may cause

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venous rupture with resultant bleeding into the subdural space on one or both sides, and accumulation of bloody effusion or subdural hematoma. This sequence may at times be visualized during operation; for example, when a lateral ventricle is emptied with suction to allow performance of choroid plexectomy; and it appears reasonable that pronounced lowering of intraventricular pressure by any procedure, including spinal puncture, may lead to the same chain of events.

Because the primary aim of therapeutic operations for hydrocephalus is reduction of intraventricular and intracranial pressure by drainage of spinal fluid[1-4] or lessening of its production rate,[5] it is clear that such operations may, if successful, be complicated by bleeding into the subdural space. Thus, in the present series subdural hematoma developed after performance of spinoureteral anastomosis[1] in one case, following choroid plexectomy[5] in the second, and in the third, subsequent to removal of a large choroid plexus cyst which had caused ventricular obstruction and internal hydrocephalus.

Report of Cases

Case 1: A 3½ mo. old girl was admitted to Childrens Hospital with history of unduly rapid

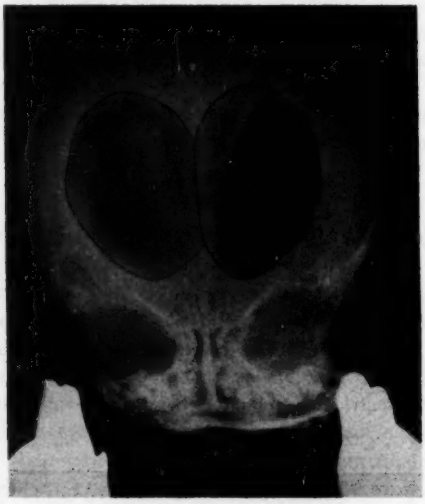

Fig. 1 (Case 1). Ventriculogram (retouched) showing enlargement of lateral ventricles and thinning of cortex in infant with communicating internal hydrocephalus.

cranial enlargement, beginning at age 4 wk., and recent vomiting and irritability. Examination showed anterior fontanelle tense and head considerably larger than normal, measuring 50 cm. in circumference, compared to sitting height of 38 cm. Subdural punctures through the coronal suture were carefully performed bilaterally, and no subdural fluid was obtained. Ventricular puncture was then performed and Evans Blue dye 5 cc. instilled; dye was promptly recovered by spinal tap. Ventriculography demonstrated large, symmetric lateral ventricles, without other deformity (Fig. 1), and it was concluded that patient had moderately advanced internal hydrocephalus of communicating type. Urologic investigation, including pyelograms, was entirely normal.

Left kidney was removed and spinoureteral anastomosis with polyethylene tube was performed

11 days later. Infant was maintained in horizontal position postoperatively, and for 10 days, the shunt functioned well; fontanelle remained soft and urine was copious and dilute. Then urinary output gradually slackened and fontanelle grew taut and bulging. Needle introduced through coronal suture encountered watery brown fluid, and this was assumed to be blood-stained cerebrospinal fluid in lateral ventricle. Evans Blue dye 5 cc. was instilled, but none was recovered from urine in 24 hr. Because the anastomosis was presumed not to be functioning, reoperation was performed and a new tube carefully installed. Fontanelle remained soft for less than 24 hr., then became tense. Operative site was again opened, disclosing no evident derangement of the tube. Tubing was relocated, wounds irrigated and closed with drains. Patient's condition was not improved following this procedure, meningitis developed, and she died 1 wk. after last operation.

Postmortem examination disclosed large bilateral unencapsulated subdural hematomas of recent appearance, completely covering and markedly compressing each cerebral hemisphere. Cortex measured only a few millimeters in thickness in many areas, ventricular system being extremely dilated. Acute, diffuse meningitis was demonstrable.

Comment: Postoperative subdural bleeding subsequent to successful spinoureteral anastomosis proved an overwhelming complication, leading to confusion in diagnosis and ultimately death of patient. Because subdural hematoma is common in infants, frequently causing symptoms and signs identical with idiopathic hydrocephalus,[6, 7] careful investigation was done before surgery to distinguish between these conditions. Neither subdural puncture nor ventriculography gave any evidence suggesting presence of subdural fluid, and preoperative diagnosis of hydrocephalus is judged to have been correct. Postoperative interpretation was, unfortunately, less discerning. Dark brown fluid obtained by needle puncture through coronal suture was erroneously assumed to represent old blood in distended lateral ventricle, although the true location and nature of fluid collection could have been readily established by dye or air studies. (See section on Diagnosis.) It was not realized that subdural hematoma could develop in these circumstances without direct instrumentation of brain.

Case 2: (Patient of Dr. G. H. Patterson.) This female infant, 3 mo. of age, was well until 5 wk. before hospitalization, when the forehead was observed to be higher and more prominent than average. Subsequently, head growth became abnormally rapid and, on admission, head circumference was 44 cm., the fontanelle large and tense. Bilateral subdural punctures were negative, and pneumoencephalogram demonstrated only marked enlargement of lateral and third ventricles. Congenital communicating internal hydrocephalus was diagnosed and choroid plexectomy recommended. Operation consisted of small R posterior parietal craniotomy, cortical incision, aspiration of cerebrospinal fluid from lateral ventricle, and cauterization and removal of all accessible choroid plexus. Ventricle was then filled with Ringer's solution, dura and scalp closed.

During the ensuing 6 wk.. head grew 2 cm. in circumference, although fontanelle remained relatively soft. Left choroid plexectomy was proposed, and craniotomy opening made in L posterior parietal region. When the dura was incised a large subdural hematoma was encountered, covering the entire L cerebral hemisphere and containing dark brown fluid, without clots. A thin internal neomembrane was excised but brain failed to expand fully, and subdural space was filled with saline solution before closure.

For 10 days patient had low grade fever but progress was otherwise unremarkable until 2 mo. later, when she was again hospitalized because of vomiting, and tenseness of fontanelle. Head had enlarged only 1 cm. during this interval, but subdural puncture yielded abundant yellow fluid bilaterally, and operation was advised. Craniotomy demonstrated a large recurrent hematoma on L side, and exposure of R side 2 wk. later revealed an extensive hematoma over this hemisphere also; removal of internal neomembrane was carried out at both operations. Saline was injected intrathecally, and drainage of subdural space maintained for 1 wk., but in both instances subdural fluid accumulated again. The child's condition deteriorated and she died about 6 mo. after last operation. Postmortem examination was not permitted.

Comment: Craniotomy for choroid plexus removal showed characteristic large ventricle and thin, flexible cortex of hydrocephalus, without evidence of subdural hematoma. Also, neither preoperative subdural punctures nor pneumoencephalography suggested such a lesion on either side. It is clear that collapse of brain during and subsequent to operation caused bleeding into the subdural space on both sides and formation of subdural hematomas. As in the preceding case, this complication proved disastrous, even though the second patient's lesion was recognized fairly early (about 6 wk.) after its inception.

Case 3: This 3½ mo. old girl had shown abnormally rapid head growth without other symptoms for 2 mo. before hospital admission. Examination showed fontanelle to be tense, head broad and larger than normal (46 cm.); sitting height was 42 cm., chest circumference, 41 cm. Although pupils constricted well to light, visual acuity appeared to be poor. Subdural punctures on 2 occasions were unproductive. Ventriculogram demonstrated a large, smooth mass, filling posterior portion of L lateral ventricle, obliteration of third, and marked dilatation of both lateral ventricles (Fig. 2).

By means of L parietal craniotomy and cortical incision, a large intraventricular cyst containing choroid plexus was visualized and removed. Cortex was observed to be thin, and care was taken to re-expand the ventricle, following relatively short operation, by instilling Ringer's solution into the ventricle before and during closure. Hemostasis was believed to be complete.

Three days later, tenseness of fontanelle prompted the operator to perform subdural punctures, and reddish-yellow fluid 15 cc. was readily obtained from each side. Bilateral subdural hematomas were suspected, and daily punctures were done for 2 wk., as much as 70 cc. of fluid being obtained

FIG. 2A and B (Case 3). Anteroposterior and lateral ventriculogram (retouched) disclosing large filling defect produced by cyst of L choroid plexus and pronounced expansion of lateral ventricles.

on occasion from R (unoperated) side. The L craniotomy was reopened, showing hemisphere to be smaller than cranial space and uniformly depressed about 1.5 cm. There was free communication between ventricle and subdural space through the open cortical incision, and no evidence of hematoma or neomembrane. Wound was closed without drainage.

Right parietal bone flap 2 wk. later revealed a well developed subdural hematoma, about 2 cm. thick, 6 cm. wide, and 12 cm. long, covering upper half of R cerebral hemisphere. Following removal of internal neomembrane, the brain was observed to expand satisfactorily before wound closure.

Convalescence was marred by wound infection necessitating sacrifice of the bone flap, but intracranial hypertension has not recurred in succeeding 4 mo., although patient's physical and mental development are slow and visual acuity is very poor.

Comment: Experience in the 1st 2 cases led to early suspicion of subdural hematoma as a complication in this patient, and demonstration of this lesion on the unoperated side of brain, as in Case 2. On the other side, subdural-ventricular communication through operative opening allowed constant circulation of spinal fluid in subdural space and possibly helped prevent formation of a hematoma. This mechanism was not effective after choroid plexectomy in the second case, though conditions were very similar.

Diagnosis

From the course of events in the cases presented, it appears subdural hematoma may develop insidiously after operative decompression of the hydrocephalic brain, producing few symptoms or signs. Fever is apt to be lacking, fontanelle may not become tense and cranial enlargement need not be excessively rapid, at least in the early stages. Appearance of these and other appropriate symptoms such as lethargy and vomiting, is delayed because the enlarging hematoma easily acquires room by depressing the brain, or by occupying dead space created through loss of cerebrospinal fluid. This holds true particularly if the surgical objective has been attained, namely, sustained lowering of intraventricular pressure.

Once the lesion is suspected, diagnosis of subdural hematoma should be relatively

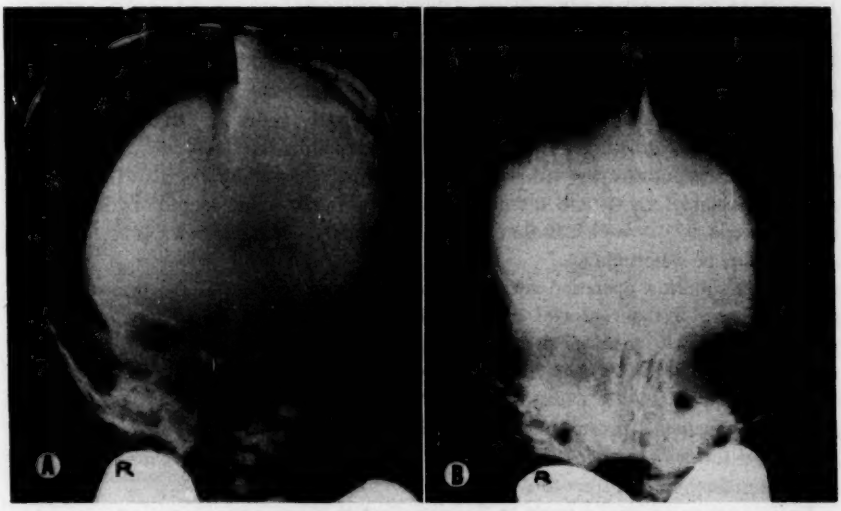

Fig. 3 (Case 2). A. Roentgenogram showing result obtained by withdrawing fluid from subdural hematoma and instilling air, in hydrocephalic infant previously subjected to choroid plexectomy. B. Demonstration of bilateral subdural hematomas in another study of same patient. Configuration of collapsed brain suggests that traction is being applied to cerebral veins entering longitudinal sinus (arrow).

simple. Dural punctures by needle through the coronal suture will disclose reddish-yellow or brown fluid in the subdural space, and this finding alone is practically pathognomonic.[6,7] Care must be taken not to advance the needle point more than a millimeter or two beyond the dura because the thin cerebral cortex is easily perforated, allowing entrance into the lateral ventricle. There is less chance of inadvertent ventricular puncture if a sizeable fluid collection is interposed between dura and brain, but should the hematoma be thin, or absent altogether, ventricle may be surprisingly close to the dura and readily penetrated.

If there be question about location of the needle, one may drain out about 30 cc. of fluid and instill a similar volume of air. Roentgenogram of the head will then disclose identity of the air-filled space, clarifying the problem (Fig. 3). An alternative method

is instillation of Evans Blue or other suitable dye 5 to 10 cc. into the cavity in question, followed immediately by puncture of the opposite ventricle. If fluid from the second needle is dye-tinged, one may presume the first is situated in ventricle rather than a subdural hematoma; conversely, if dye does not appear it is probable the initial needle rests in the subdural space. This method is apt to be less accurate than air injection, and requires that communication between lateral ventricles has been previously demonstrated.

Prevention

Incidence of postoperative subdural bleeding in hydrocephalic patients may be lowered by careful consideration of certain technical aspects of the surgical procedures. For example, it is desirable not to cause sudden and profound lowering of intraventricular pressure in the course of operation. This is unavoidable during choroid plexectomy, when one lateral ventricle must be entered and its fluid temporarily removed, but ill effects of sudden decompression can be reduced and the chance of subdural effusion lowered, by utilization of measures which will re-expand the ventricle before closure. As Voris pointed out,[8] it is important to completely refill the collapsed ventricle with spinal fluid or Ringer's solution, thereby expelling air from the ventricle and pressing cortex outward toward the dura, narrowing the subdural space. If the brain does not expand fully, it will often be desirable to instill saline solution by slow intrathecal injection[9,10] as well. Absolute hemostasis must be obtained, and it is essential that dural closure be watertight.

When a shunting operation such as spinoureteral anastomosis is performed, sudden severe collapse of the ventricles does not occur because cerebrospinal fluid is released much more slowly than in performance of choroid plexectomy. Nevertheless, it is obvious from Case 1 that even slow drainage of spinal fluid through a polyethylene tube of 1 mm. bore does not necessarily preclude cerebral shrinkage, venous rupture, and subdural hemorrhage. It can be reasonably assumed, however, that rate of decompression is a critical factor in the equation, and an operation which lowers intraventricular tension slowly must be preferred from this standpoint.

Two additional factors having to do with control of intracranial pressure are position of the patient following operation and his state of hydration. As the head is elevated, pressure within the cranium becomes reduced, particularly if tube drainage of any sort is functioning. In view of this, it is wise to maintain the patient in horizontal or Trendelenburg position for 10 days following operation, and gradually elevate the head of the bed after this interval. In the early postoperative period, the baby should be turned frequently but cautiously, guarding against jarring or quick movement of the head. Dehydration must be avoided by providing for normal or increased fluid intake, depending upon measured fluid and electrolyte excretion. All nutritional elements should be adequately supplied and normal blood count maintained by transfusion whenever this is necessary.

Treatment

A subdural hematoma which develops after operation for hydrocephalus may demand more elaborate treatment than is usually required for this lesion, because circumstances favor a tendency to recurrence. Preliminary decompression is carried out for 7 to 10 days by daily subdural puncture[7] and withdrawal of 20 to 40 cc. of fluid,

alternate sides being tapped on successive days. Except in an occasional early case, cured by aspirations, osteoplastic craniotomy should then be performed on one side, subdural fluid removed by suction and irrigation, and internal neomembrane of the hematoma removed. Minute attention to hemostasis is absolutely essential. The subdural space must be obliterated, if possible, by means of intrathecal or intraventricular injection of saline solution, supplemented when necessary by subdural irrigation with distilled water, and intravenous administration of water or half-normal saline.[10] A subdural drain may be left in place for a few days if dead space cannot be eliminated, provided no opening exists into the ventricle and careful precautions are taken to forestall infection.

In an infant with bilateral hematomas, it would seem wise to defer craniotomy on the other side for at least two weeks, maintaining the patient horizontal or with head dependent. During this interval subdural puncture on the operated side should be performed 2 or 3 times to demonstrate or exclude recurrent bleeding, and the opposite subdural space cautiously decompressed by needle about twice weekly. Surgical and postoperative precautions above described apply, of course, when craniotomy is undertaken on the second side.

When the brain has been distorted and functionally impaired by hydrocephalus, it poorly tolerates repeated surgical trauma and compression by space-taking lesions. Hence, if subdural hematoma is not prevented from developing subsequent to operation, this destructive complication should at least be identified early and treated with dispatch.

Conclusions

Report is presented of three infants in whom subdural hematoma developed as a consequence of surgical treatment for hydrocephalus. This complication was not recognized in the first patient, and was unsuccessfully dealt with in one of the others.

Anatomic and physiologic features predisposing to subdural bleeding in hydrocephalic patients are outlined, and methods of prevention, diagnosis, and therapy are described.

Success of operation is jeopardized and likelihood is increased of subsequent blindness, convulsions, and mental impairment in a hydrocephalic infant whose precariously adjusted brain is further damaged by this development.

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SPANISH ABSTRACT

Hematoma subdural como complicación del tratamiento quirúrgico de la hidrocefalia

De 24 lactantes en los que se hizo el tratamiento quirúrgico de su hidrocefalia interna congénita, tres presentaron hematoma subdural en el período postoperatorio temprano.

En el primer caso el estudio postmortem demostró la existencia de un gran hematoma subdural bilateral de aspecto reciente, que no estaba encapsulado, y cubría por completo cada uno de los hemisferios cerebrales a los cuales comprimía en forma acentuada. Simultáneamente existía una meningitis aguda difusa. En este enfermo se hizo una anastomosis espino-ureteral y el hematoma bilateral no fué sospechado dada la ausencia de manejo de tejido cerebral. En el segundo enfermo en que se realizó la extirpación del plexo coroide del ventrículo derecho, el diagnóstico del hematoma bilateral se hizo por punciones repetidas y craneotomía, primero de un lado y después del otro, con extirpación de las membranas internas; no hubo mejoría del enfermo terminando con su muerte. En el tercer caso se realizó la extirpación de un quiste intraventricular que contenía plexos coroides; se sosperchó el desarrollo del hematoma en el lado sano y se comprobó por punción subdural y por craneotomía. Se logró hacer la extirpación de la membrana interna observándose una expansión correcta del cerebro antes de cerrar la herida. En este enfermo el procedimiento tuvo éxito ya que no hubo recaída de la hipertensión intracraneana en los próximos cuatro meses pero el desarrollo físico y mental del niño fué muy lento y la agudeza visual quedó seriamente disminuida. Es interesante señalar que en este caso la comunicación ventricular subdural establecida por el acto quirúrgico impidió posiblemente el desarrollo del hematoma en el lado operado, sin embargo, en el segundo caso no lo evitó.

El mecanismo por el cual se producen dichos hematomas se cree que sea el siguiente: al hacerse la descompresión intraventricular por la salida del líquido cefaloraquídeo en el momento de realizar la operación, se produce un colapso de la corteza cerebral, que por el efecto compresivo del proceso hidrocefálico ha quedado reducida a una capa mínima de tejido nervioso, quedando suspendida de las venas cerebrales superiores que salen a intervalos irregulares del borde superior y mediano de cada hemisferio y que van a desembocar al seno longitudinal y de las que emergen del borde inferior y lateral de los lóbulos temporal y occipital que desembocan en el seno lateral; por gravedad la corteza hace tracción sobre las mismas, tracción que se supone sea mayor entre mas rápida sea la evacuación del líquido. la duración de la descompresión y el crecimiento del craneo, produciendose finalmente su ruptura lo que determina la hemorragia en el espacio subdural.

El desarrollo del hematoma se acompaña de escasos síntomas o signos y puede hacerse en forma muy insidiosa, instalándose lentamente el cuadro clínico franco debido a que éste no se manifiesta ruidosamente hasta que es lo suficientemente voluminoso para ocupar el espacio mas o menos grande que ha dejado la descompresión ventricular y ha favorecido la macrocefalia y producir fenómenos de compresión cerebral.

Es posible que no exista fiebre, aumento de tensión de la fontanela, ni tampoco crecimiento rápido del craneo cuando menos en su principio, máxime si el tratamiento quirúrgico produjo una disminución permanente de la presión intraventricular. Pero lo importante esta en pensar y sospechar la existencia de la complicación pues el diagnóstico definitivo se realiza fácilmente por punciones subdurales a través de la sutura coronaria que permitirá obtener del espacio subdural un líquido amarillo rojizo u obscuro y este hallazgo por si sólo es prácticamente patognomónico.

Se recomienda para su prevención, si se practica plexectomía coroidea hacer la reexpansión de los ventriculos colapsados con líquido cefaloraquídeo o solución de Ringer y aún, si ésta no es completa, inyectar lentamente solución salina isotónica por vía intratecal; y hacer impermeable al agua la sutura de la dura madre, y hemostasis perfecta. Es también aconsejable mantener al niño en posición de Trendelenburg durante diez díaz después de la operación, principalmente en cualquier tipo de operación con tubo de drenaje, y elevar la cabeza gradualmente después de este tiempo, durante el cual deben evitarse movimientos violentos de la cabeza aunque es conveniente cambiar al niño de posición frecuentemente pero con precaución. Otro factor que no debe descuidarse es mantener una correcta hidratación del paciente.

El tratamiento es mas laborioso que en hematomas subdurales de otro tipo por las circunstancias que favorecen su recidiva: punciones repetidas, cranietomías osteoplásticas con extirpación de la membrana interna etc. etc. son las medidas usadas en la actualidad.

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ADRENOGENITAL SYNDROME IN A MALE CHILD DUE TO ADRENOCORTICAL TUMOR

Report of Case with Hemihypertrophy and Subsequent Development of Embryoma (Wilms' Tumor)

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Beverly Hills, Calif.

THE adrenogenital syndrome in childhood after the neonatal period is most frequently produced by an adenoma or carcinoma of the adrenal cortex. The etiology is not known, but symptoms may be explained by increased androgenic hormonal activity of the adrenocortical tumor.[1-10] The clinical picture is characterized by hirsutism, increased size of the external genitalia, deepening of the voice, advanced muscular and somatic development and, frequently, acne and accelerated bone age. In males, the penis and scrotum may enlarge markedly, but the testicles remain small and immature. Urinary 17-ketosteroids are elevated and an adrenal tumor may be palpable.

Cases due to adrenocortical tumor may usually be differentiated from those due to congenital adrenocortical hyperplasia by the absence of pseudohermaphroditism in females, familial occurrence and symptoms of Addisonian crises. However, adrenogenital syndrome due to tumor may be clinically identical to verified cases[11-14] due to postnatal adrenocortical hyperplasia without signs of adrenocortical insufficiency. Since treatment consists of surgical removal of the adrenocortical tumor, all cases in which the diagnosis of adrenocortical tumor is suspected merit exploratory laparotomy.

The relative frequency and sex incidence in children of adrenogenital syndrome produced by adrenocortical tumor is suggested by Wilkins' tabulation[10] of 41 reported cases with 29 females and only 12 males.

The purpose of this paper is to report the case of a boy with adrenogenital syndrome due to adrenocortical tumor with the unusual association of hemihypertrophy and the subsequent development of an embryoma (Wilms' tumor); and to summarize briefly the cases reported of male children with adrenogenital syndrome due to adrenocortical tumor.

CASE REPORT

J. C., an 11 mo. old white male infant, was admitted to Children's Hospital because of progressive hirsutism and enlargement of genitalia. Parents were American-born and in good health. Patient, an only child, was a normal, full-term infant at birth weighing 4.8 kg. and measuring 62 cm. Development and appearance were apparently normal until 5 mo. of age when excess hair appeared on the face, shoulders, back and extremities. During the following 2 mo., penis increased noticeably in size and hair appeared in pubic and anal regions.

Physical Examination: Pulse rate 110/min., B.P. 110/80 mm.Hg, weight 12.2 kg., height 74 cm. Patient was well-nourished and sturdy with advanced somatic and sexual development of the typical "Little Hercules" (Fig. 1). Voice was deep and husky. Thick curly black hair covered his

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head and eyebrows were thick and dark. A growth of fine hair was present on face, trunk and extremities and a generous growth of coarse hair covered pubic and perianal regions. Penis and scrotum were markedly enlarged, but testicles did not appear overdeveloped. An ovoid mass, approximately 3 cm. in diameter, firm and not readily movable, was palpated deep in R upper abdominal quadrant. Heart and lungs were normal. Ocular fundi were normal and there were no abnormal neurologic findings.

Laboratory Data: Hgb. 13.6 gm./100 cc., RBC 5 million/cm., WBC 7.5 thousand/cmm. with

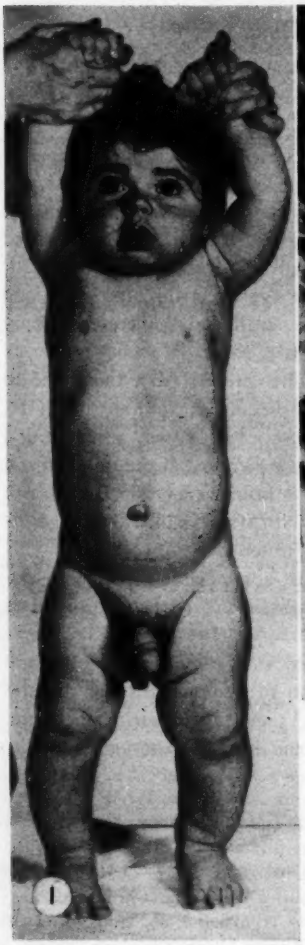

FIG. 1. Patient at 11 mo. showing hirsutism, advanced somatic development and enlarged genitalia.

FIG. 2. Microscopic section of adrenocortical adenoma.

35% polymorphonuclears, 49% lymphocytes and 16% monocytes. Repeated urine examinations were within normal limits. Blood cholesterol was 177 mg./100 cc. Urinary 17-ketosteroids were elevated to 15.9 mg. (Normal for adult male 8 to 22 mg./24 hr. and for male infant less than 0.5 mg./24 hr.[15, 18]) Roentgenograms of skull, chest and long bones were normal with no acceleration of bone age. Retrograde pyelography demonstrated only slight blunting of calyces of L kidney.

Diagnosis: Probable tumor of R adrenal cortex.

Operation: Following prophylactic administration of adrenal cortical extract, surgery was per-

formed and a rounded tumor mass of R adrenal gland was found and removed. Left adrenal gland and other abdominal organs appeared normal. Initial postoperative course was stormy with marked restlessness, hyperpyrexia, tachycardia and hypertension. After 48 hr. general condition improved dramatically and the remainder of convalescence was uneventful. He was discharged in good condition 3 wk. after surgery at which time the urinary 17-ketosteroids were reduced to 4.2 mg.

Pathologic Examination: Grossly, specimen measured 3.6 x 3 x 2.5 cm. and was surrounded by fibrous tissue. Structure and consistency of tumor was uniform throughout with no areas resembling normal adrenal tissue. Microscopic sections (Fig. 2) revealed tumor cells consisting chiefly of cords of cells bearing closest resemblance to cortical cells of the zona reticularis. There were some larger vacuolated cells with nuclei pushed to the margin. Staining with Sudan IV produced a red color. The foamy-appearing cells contained the largest amount of fat, but almost every cell in the section contained some fat-staining material.

Diagnosis: Adenoma, R adrenal cortex, benign.

Interval Course: Considerable regression of hirsutism was apparent 1 mo. after surgery and behavior was described as more infantile than formerly. He was readmitted to hospital at 18 mo. of age for observation. At this time, hair on his head was lighter in color, less curly and finer in texture. Most of the body hair had disappeared with the exception of a small amount on the back and in the pubic region. Voice had reverted to normal and heavy musculature showed partial regression. No demonstrable change was noted in actual size of penis and scrotum (Fig. 3). Urinary 17-ketosteroids were 3.2 mg. A significant observation hitherto unnoticed was an asymmetric development or hemihypertrophy of L arm and leg; both were slightly longer than the corresponding R arm and leg. In retrospect, measurements of photographs and roentgenograms established the presence of hemihypertophy when he was first examined at 11 mo. of age.

Examinations during next 4 yr. indicated that growth and development had followed a reasonably normal pattern, although the boy was obviously large for his age. His general behavior was considered normal and at no time did he evince any unusual sex interest. Left-sided hemihypertrophy persisted, but was mild. At 4 yr. of age he walked with a limp and had to wear a size larger shoe on L foot. Left leg was about 1.2 cm. longer than R. Difference in circumference of thighs was 2.0 cm.; of calves 1.5 cm.

Readmission at 5¾ Years of Age: After an absence of 3 mo. from clinic, a routine examination disclosed a large abdominal mass occupying most of R upper quadrant. The only complaints elicited were occasional mild abdominal discomfort and constipation. Weight 22.7 kg., height 122 cm., blood pressure 120/70 mm.Hg. Genitalia, scant pubic hair and asymmetry of extremities were essentially unchanged. The only new significant finding was the abdominal mass which was firm, nodular, nontender and movable; extending down to R anterior superior iliac spine and to L of umbilicus (Fig. 4). Blood and urine examinations were normal. NPN ranged from 31 to 40 mg./100 cc. Urinary 17-ketosteroids were 3.0 mg. Intravenous pyelogram revealed large pelves with R pelvis distorted and pushed upward and outward. Right ureter was deflected to right. Chest RGs and long bones revealed no metastases or other abnormalities.

A diagnosis of embryoma, neuroblastoma or other retroperitoneal tumor was suspected.

Second Operation: At surgery, the large abdominal tumor involving upper and middle portions of R kidney was excised with R kidney en masse. Convalescence was uneventful. A course of roentgen therapy (150 R for 20 days) was begun postoperatively and completed before patient was discharged.

Pathologic Examination: Grossly, specimen was an oval mass of tissue measuring 8.8 x 13.8 x 16.4 cm. and consisting of a large tumor and R kidney. On cross-section of kidney, the renal cortex and pyramids were distinctly made out. Main tumor mass felt almost cyst-like and, on section, was composed of soft tumor tissue. Microscopically, tumor showed a varying structure (Fig. 5). One section through main tumor mass contained tubular-like acini packed closely together. Between these abnormal tubules were strands of myxomatous tissue. Occasional mitotic figures were present. Other sections contained deep-staining cells in circumscribed islands separated by loose myxomatous-type tissue. Mitotic figures were more abundant in these areas. Some tumor cells showed early necrosis with pyknotic changes in the nuclei. Sections of kidney showed normal appearing renal structure. At the margin of one section of kidney was definite tumor tissue. In none of the sections was there any evidence of adrenal tissue or inflammatory reaction.

Diagnosis: Adenomyosarcoma, region of R kidney, with invasion of kidney.

FIG. 3. Patient at 18 mo. showing operative scar and marked regression of hirsutism. Mild left-sided hemihypertrophy first observed at this time.

FIG. 4. Patient at 5¾ yr. showing outline of embryoma.

Subsequent Course: During the next 5 mo. he was observed in the Out-Patient Clinic at monthly intervals and progressed satisfactorily. Roentgen examination of the chest 6 mo. after surgery revealed 2 dime-sided areas of increased density in R lung field. These were believed to be metastatic. A marked progression of these nodules was noted during the next 6 mo. with no metastases noted elsewhere in the body. He became dyspneic 14 mo. postoperatively and began to fail rapidly. He was readmitted to hospital for 1 wk. with a collapse of R lung and a partial collapse of L lung. Although near the end of his disease, he was permitted to return home where he died on his 7th birthday.

Postmortem Examination: Only additional positive findings are included. Grossly, R pleural cavity was completely obliterated by soft, cellular tumor tissue adherent to all parietal surfaces and containing numerous cavitations. Heart was pushed over to L side. Left lung was compressed and contained firm tumor nodules averaging 7 mm. to 1.5 cm. in diameter. Except for these nodules, pulmonary parenchyma of L lung appeared normal. Both adrenals were located, L weighing 5.5 gm. and R 2.0 gm. Microscopically, sections through tumor tissue in the lungs showed areas of loose fibrillary background in which oval to cylindric nuclei were noted; also bundles of nuclei which resembled smooth muscle. Mitotic figures were fairly abundant. Some areas showed marked edema, hemorrhage and necrosis. Sections through adrenals were not remarkable; testicles revealed no evidence of spermatogenesis.

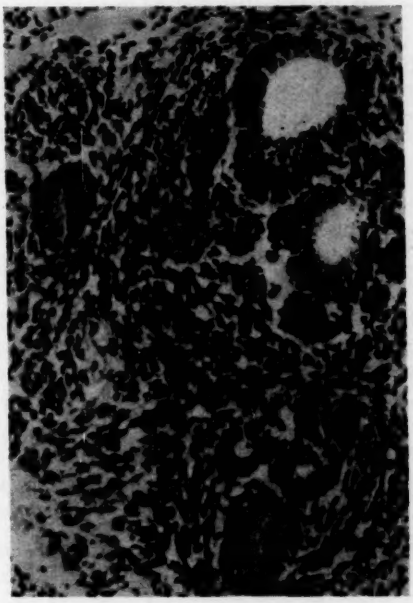

FIG. 5. Microscopic section of adenomyosarcoma.

Final Diagnosis: 1. History of adrenogenital syndrome with removal of adrenocortical adenoma; 2. History of removal of adenomyosarcoma with right kidney; 3. Adenomyosarcoma, metastases in both lungs.*

DISCUSSION

No record was found in the literature of adrenogenital syndrome associated with embryoma. The present case had apparently responded well to the successful removal of an adrenocortical adenoma at one year of age with dramatic regression of hirsutism, reversion of the deep voice and marked diminution of urinary 17-ketosteroids. A large abdominal tumor was discovered near the site of original surgery almost five years later on routine physical examination. There was no clinical evidence of a recurrence of adrenocortical tumor with either androgenic symptoms or elevated urinary 17-ketosteroids.

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* For the pathologic reports in this paper, the author is indebted to Dr. Ralph Knutti.

What relationship, if any, exists between the adrenocortical tumor and the subsequent development of the embryoma is a matter of conjecture. It may be only coincidental that both tumors occurred on the same side, but the derivation of the adrenal cortex in the developing embryo from a bud of mesodermal cells next to the mesonephros suggests the possibility of a common etiologic factor relating these tumors.

Another rare feature in this case is the mild left-sided hemihypertrophy. Hutchison[17] in 1904 first reported the unusual association of hemihypertrophy with adrenal pathology in a four month old male infant with left-sided hemihypertrophy since birth involving the soft tissues of the extremities and trunk. Following death, his paired organs were found to be asymmetric with the left adrenal gland three times heavier than the right and weighing 42 gm.

Harwood and O'Flynn[18, 19] reported the case of a boy with right-sided hemihypertrophy associated with virilism and a large right-sided adrenocortical tumor. Because both the tumor and the hemihypertrophy occurred on the right side, the hypothesis was made that either the tumor may have been part of the hemihypertrophy or the tumor may have caused the hemihypertrophy "as an example of a predominantly unilateral effect of hormones secreted in the circulating blood by the cortical cells." This interesting explanation could be considered in the cases reported by Hutchison and by Harwood and O'Flynn with hemihypertrophy and isolateral adrenal disturbances, but not in the present case in which hemihypertrophy occurred on the side opposite to the adrenocortical tumor.

Also of interest is the case of hemihypertrophy reported by Kottmeier[20] in which he demonstrated calcium deposits above both kidneys on roentgen examination. There is no satisfactory explanation for the asymmetric development in these cases except that it probably originated in early embryonic development with unequal segmentation of the ovum.

Further studies on the dynamics of embryologic development of tissues and organs and their relation to steroid metabolism may help to explain not only associated anomalies or malformations, but also the malignant tendency and the high incidence in females of adrenocortical tumors.

Review of Cases

Twenty-two cases of male children with adrenocortical tumors and symptoms of adrenogenital syndrome are reviewed, including the present case, one unpublished case from the Children's Hospital in Los Angeles and 20 cases[18, 19, 21–40] reported in the literature. All but the case of Rowntree and Ball[30] were substantiated by tumor specimen or postmortem examination. Symptoms were present under 1 year of age in 9 cases and under 3 years of age in 18 cases. Of special interest are the two cases of Weber and Menten[37] and of Lowry and Brown[40] with symptoms present at birth, because hyperadrenocorticism with recognizable symptoms at birth is usually associated with congenital adrenocortical hyperplasia rather than with adrenocortical tumor. A palpable tumor was described in 13 cases and roentgen evidence suggestive of a tumor mass was present in four additional cases in which a mass was not palpable. Urinary 17-ketosteroids were elevated in all seven in which the determination was done.

The operative record indicates that only 5 of the 10 cases reported between 1903, when Linser[21] presented the first case, and 1933 were operated upon with one recovery; all 12 cases subsequently reported had surgery with six recoveries. The author's case is

included as one improved on the basis of clinical response to the original surgery and the assumption that the child's death six years later was due to metastases from a complicating embryoma. The tumors occurred on the left side in 10 cases and on the right in 12 cases; their weights varied between 37 and 6800 gm. A high degree of malignancy is shown by the pathologic reports of 12 malignant tumors with metastases present in eight cases.

The case reported by Reilly[36] illustrates diagnostic and prognostic difficulties which may be encountered. This six year old boy recovered following surgery after a "stormy" course complicated by shock and hemorrhage. A large encapsulated tumor removed at operation was described pathologically as a "degenerated adrenal adenoma." Although his general condition remained good, he continued to have signs of increased androgenic activity four years after surgery with elevated 17-ketosteroids, accelerated bone age and advanced somatic development. Wilkins[10] in his recent book suggested that this case was probably one of congenital adrenal hyperplasia with adenomatous changes and hemorrhage resulting in adrenal crisis.

Summary

A rare case of adrenogenital syndrome due to adrenocortical tumor is reported in a male child with left-sided hemihypertrophy and the subsequent development of an embryoma.

Marked regression of hirsutism, advanced somatic and muscular development, deep voice and elevated urinary 17-ketosteroids followed removal of an adrenocortical adenoma. An embryoma was discovered five years later near the site of original operation. Removal of this tumor was followed by metastases and death after 15 months.

The unusual association of adrenogenital syndrome with hemihypertrophy and embryoma is discussed. This case serves to emphasize the need for a guarded prognosis and alert observation even years after an uneventful course following removal of an adrenocortical tumor.

A brief review is presented of 22 cases of adrenogenital syndrome in male children with adrenocortical tumors including the above case.

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SPANISH ABSTRACT

Síndrome adrenogenital en la infancia

Con el caso aquí relatado son 21 los casos de síndrome adrenogenital reportados en la literatura.

Se trataba de un niño de 11 meses de edad cuyo desarrollo fué normal hasta los 5 meses cuando se apreció una cantidad excesiva de pelo en la cara, hombros, espalda y extremidades y en los 2 meses siguientes aumento notable del tamaño del pene y desarrollo de pelo en el pubis y región peri-anal. Al examinarlo se notó voz profunda y gruesa, el exceso de pelo citado, pene y escroto grandes y testículos de tamaño normal. En el cuadrante abdominal superior derecho se encontró una tumoración firme, poco movible y ovoide, situada profundamente. Sus 17 ketosteroides urinarios fueron de 15.9 mlgs./24 hs, en contra de la cifra normal de 0.5 mlgs. No había aumento en su edad ósea. La pielografía retrógrada enseñaba solo cálices del riñón izquierdo ligeramente romos. En la intervención quirúrgica se encontró dicho tumor que al estudio histológico resultó ser un adenoma benigno de la corteza suprarrenal.

A los 18 meses todos los síntomas con excepción del pene y escroto que permanecían de igual tamaño habían practicamente desaparecido, los 17 ketosteroides urinarios bajaron a 3.2 mlgs, pero por primera vez se apreció hemihipertrofia izquierda que afectaba el brazo y piernas, miembros que eran mas largos que los opuestos, pero que ya estaba presente desde los 11 meses y había pasado desapercibida.

A la edad de 5 años 9 meses, se le encontró un gran tumor abdominal situado en el cuadrante superior derecho sin mas síntomas que cierta molestia abdominal y constipación. La pielografía intravenosa reveló pelvis renal derecha distorsionada y rechazada hacia arriba y afuera. Se hizo su extirpación quirúrgica y el estudio histopatológico reportó tumor de Wilms.

Murió a los 7 años con metástasis pulmonares que aparecieron a los 6 meses de la operación no obstante 3000 r dados después de ésta. La autopsia confirmó la presencia de metástasis pulmonares con suprarrenales normales.

Es posible que haya sido simple coincidencia la presencia de ambos tumores en el mismo lado pero el origen de la corteza suprarenal de un mamelón de células mesodérmicas cerca del mesonefro sugiere la posibilidad de un factor etiológico común.

En lo rèferente a la hemihipertrofia la explicación mas plausible es la de que sea determinada por una segmentación asimétrica del óvulo.

Este síndrome adrenogenital, producido por el aumento de la actividad hormonal androgénica de un tumor adrenocortical, puede diferenciarse generalmente de los debidos a simple hiperplasia congénita de la corteza suprarrenal por la ausencia de pseudo hermafroditismo en las mujeres, su carácter familiar y el cuadro de crisis addisonianas. Sin embargo, estas últimas pueden faltar en casos de hiperplasia adrenocortical postnatal, por lo demas clínicamente idénticas a las de tumor. La predominancia de estos tumores en la mujer es mas del doble que en el hombre.

La revisión del autor de 22 casos de tumor adrenocortical demuestra que 9 presentaron sus síntomas antes del año y 18 antes de los 3, registrando dos casos en que se encontró presente al nacimiento. En 13 se tocó el tumor y en 4 mas se demostró radiológicamente.

Los 17 ketosteroides estuvieron elevados en todos los 7 casos en que se determinaron. En un primer grupo de 15 tumores extirpados hubo una curación y en otro de 12 casos, 6 aliviaron. La frecuencia de la malignidad del tumor es evidente pues de 12 casos malignos 8 dieron metástasis.

9615 Brighton Way

EXPERIMENTAL USE OF METHYL TESTOSTERONE AND TESTOSTERONE IN PREMATURE INFANTS

By HORST A. AGERTY, M.D., AND JOSEPH N. SEITCHIK, M.D.
Philadelphia

ANDROGEN therapy of premature infants has been suggested because of the protein-anabolic potential of these compounds. Shelton and co-workers[1-3] observed an increased rate of weight gain of premature infants receiving androgens. Hardy and Wilkins,[4] Reilly and Earle[5] and the authors were unable to corroborate the initial, favorable clinical reports.[6]

The present authors' initial study was continued for two reasons. First, the protein content of the diet originally offered the infants was relatively low (1.7%). Second, the only form of androgen used was methyl testosterone as crushed tablets, administered orally. With the knowledge that the protein-anabolic effect of androgens is optimal in children and adults in the presence of a high protein intake and that nothing is known of the gastrointestinal absorption of methyl testosterone by premature infants, it was believed that the original experimental situation might not permit the maximum opportunity for demonstration of a protein-anabolic effect in premature infants. The study was therefore re-designed to include a group of infants on a high protein diet and the administration of methyl testosterone orally in a liquid carrier and of testosterone suspension by injection.

METHOD

A total of 100 premature infants weighing between 1.8 and 2.3 kg. have been studied. Androgen therapy was begun 48 hr. after delivery and continued throughout the study. The infants were housed for the most part in Gordon Armstrong incubators and received oxygen routinely for several days. After an initial starvation period of 24 or 48 hr. following birth the infants were fed a dextrinmaltose 5% solution for 24 hr. This was followed by a formula containing 43 cal./100 cc. for 3 days, which was then increased to 66 cal./100 cc. One relatively low protein formula (1.7%)* and 2 relatively high protein formulas (4.0† and 4.1%‡) were utilized. Since these formulas individually showed no significant differences in results obtained, the figures obtained from these are grouped together. The infants were allowed to feed ad libidum. The daily dosage of androgen therapy consisted of either methyl testosterone 5.0 mg. as crushed oral tablets or dissolved in propylene glycol, or testosterone 5.0 mg. in suspension hypodermically. Both groups of infants received ascorbic acid.

The infants were studied in respect to time to regain birth weight, time to gain to 2.5 kg., rate of weight gain and protein-nitrogen intake.

RESULTS

The observations made on the control and treated infants are recorded in table 1 and

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* Similac®, M & R Laboratories, Inc.
† Dryco®, The Borden Co.
‡ Alacta®, Mead Johnson and Co.

charts 1 and 2. These results demonstrated that neither the diet nor the route of the administration of the androgen had any significant clinical effect. The treated infants were able to gain weight at least as well as the control infants on a slightly lower nitrogen intake.

Discussion

The observations recorded in this and in the authors' previous study suggest that there may be a minimal protein-anabolic effect in premature infants treated with androgens. The ability of the treated infants to gain as well as the control infants on a slightly lower nitrogen intake, as well as the slightly improved nitrogen utilization in the treated infants demonstrated in the previous study suggest this. The order of the effect is small and is associated with a slightly decreased nitrogen intake in the treated infants. Therefore

TABLE 1

Premature Infants Weighing 1.8–2.5 kg.

	1.7% protein formula		4.0–4.1% protein formula	
	Control	Testosterone	Control	Testosterone
No. infants	32	43	13	12
Av. wt. at birth (kg.)	2.1	2.1	2.2	2.1
No. days to regain birth weight	7.6	7.5	10.7	8.2
No. days to attain 2.5 kg.	19.8	17.5	17.2	17.2

Results with androgens in 1.7% protein formula series are combined values from both oral and parenteral administration of testosterone, there being no significant differences.

no clinical benefit results. We may hypothesize that either the kidney and liver enzyme systems (arginase?) in premature infants are limited in their response to androgens or that accelerating the rate of this one phase of protein synthesis cannot influence the over-all rate of protein-anabolism.

Inasmuch as no peripheral androgenic effects were noted, no conclusions can be drawn as to the relative efficiency of the various routes of administration. However, it can be stated that no one method of administration produced any significant protein-anabolic effect.

Summary

One hundred premature infants weighing between 1.8 and 2.3 kg. were studied in respect to time to regain birth weight, time to gain to 2.5 kg., rate of weight gain and protein-nitrogen intake. Fifty-five received an androgen either orally or parenterally. The infants received a diet of varying protein content.

While the results suggested a minimal protein-anabolic effect in all the treated infants, this was associated with a decreased nitrogen intake. Thus no clinical benefit resulted.

Neither the method of administration of the androgen nor the protein content of the diet offered influenced the results.

Acknowledgments

The authors wish to thank Miss Dorothy Rush, R.N., for her able assistance. The authors also wish to thank Roche Organon Co. for their generous supply of methyl

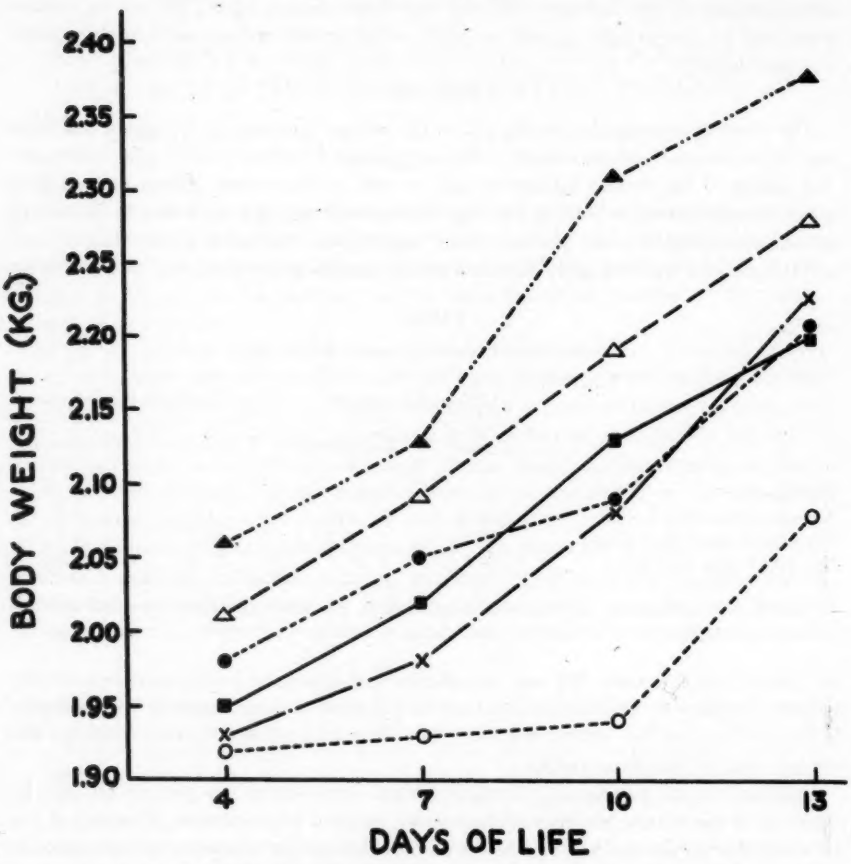

CHART 1. Body Weight (kg.)—Weight curve beginning on 4th day of life. Each line represents average figures for all cases in respective series.

○ High protein formula—control

● High protein formula—treated testosterone—(H)

△ Low protein formula—control

▲ Low protein formula—methyl testosterone orally

■ Low protein formula—testosterone propylene glycol

× Low protein formula—testosterone (H)

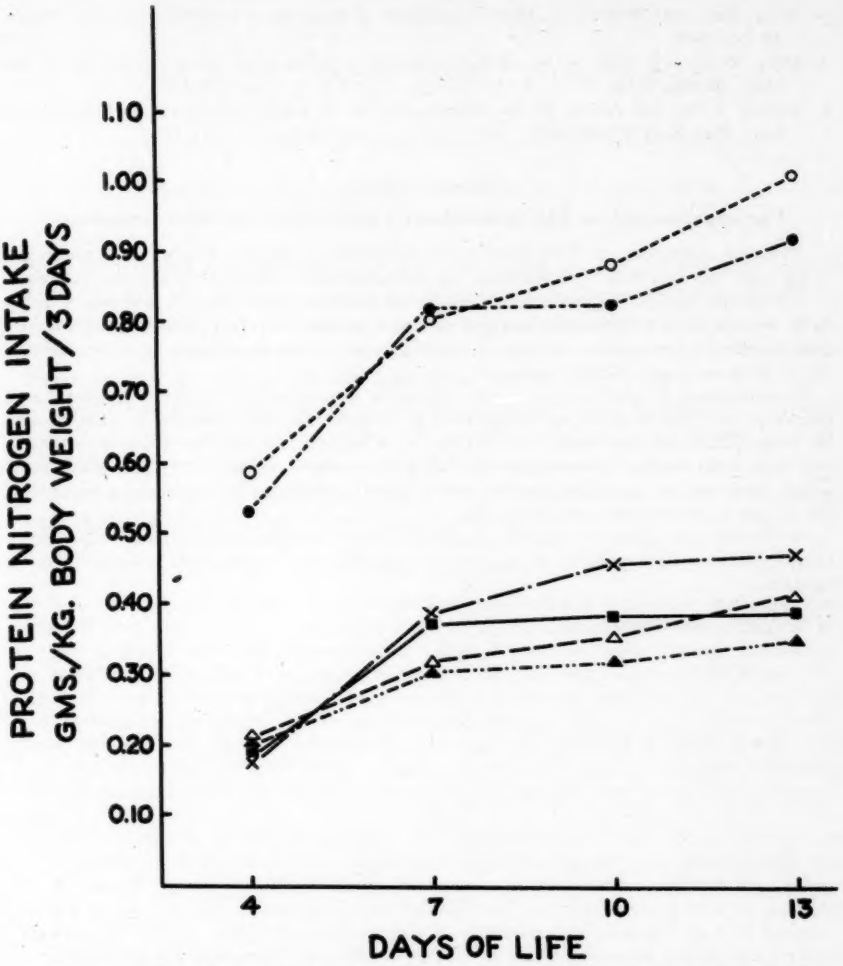

CHART 2. Protein Nitrogen Intake. Nitrogen intake recorded from 4th day of life. Each line represents average figures for all cases in respective series. For legend, see chart 1.

testosterone (neo-hombreol®) and the Schering Corporation for their generous supply of testosterone, aqueous suspension.

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SPANISH ABSTRACT

Uso experimental de Metiltestosterona y testosterona en niños prematuros

El uso de andrógenos con el fin de aumentar rápidamente la ganancia de peso de los prematuros es discutible pues aún no se han corroborado los resultados clínicos iniciales que parecían favorecerlo.

Este estudio varía de los anteriores en que se administraron dietas ricas en proteínas, 4 grs.% de la fórmula láctea y metiltestosterona por vía oral e intramuscular para librar la posible barrera gastrointestinal del prematuro y permitir al máximo la oportunidad de demostrar la acción anabólica que se le ha supuesto a dichos compuestos.

En consecuencia se administraron 5 mlgs. diarios de testosterona por vía oral o parenteral a 55 prematuros de 2 dias de edad y se tomaron otros 45 de igual edad como controles. En ambos grupos los pesos iniciales oscilaban entre 1.8 y 2.3 kgs. y se comparó el número de días que necesitaron para llegar a los 2½ kgs. encontrándose que fué prácticamente el mismo (17.5) para ambas series y para ambas vías de administración tanto para el grupo control que se le administraron fórmulas con 1.7 grs.% de proteínas como al de 4%.

Se concluye que aunque los resultados sugieren un efecto anabólico proteíco mínimo, éste estuvo asociado con una disminución en la ingestión de nitrógeno y no se obtuvieron resultados clínicos benéficos.

1111 North 63rd Street

VITAMIN A DEFICIENCY: CASE REPORT

Unusual Manifestations in a 5½ Month Old Baby

By DAVID CORNFELD, M.D.,* AND ROBERT E. COOKE, M.D.
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MOST of the signs of vitamin A deficiency noted in animals have been observed in humans. However, certain manifestations have been described either infrequently or not at all in man. Furthermore, avitaminosis A has been noted rarely in infancy because of the usual practice of feeding milk of animal origin, and the signs of deficiency at this age may be different from those noted in older children.

The following case report is that of a baby maintained on an artificial diet containing no fats of animal origin and to whom only crystalline vitamin D and ascorbic acid were regularly given as vitamin supplements. The infant presented certain signs of vitamin A deficiency which are classical in humans[1-4] and, in addition, signs hitherto observed only in experimental animals fed diets lacking vitamin A.[5-11]

CASE REPORT

S. S. was a 5½ mo. old white female on the University Service of Grace-New Haven Community Hospital from Aug. 1 to 21, 1950. Mother had had 3 previous pregnancies. Each sibling had been slightly jaundiced after birth, but subsequent course of each was benign. Patient was born at a neighboring hospital after a pregnancy characterized by good health and excellent dietary intake. Delivery was normal and spontaneous and birth weight was 2.4 kg. About 1 hr. after delivery infant was noted to have respiratory distress and to be icteric. Blood examination revealed RBC 4.2 million/cmm. and Hgb. 15.0 gm./100 cc. Blood smear contained 410 nucleated RBC cells/100 WBC. Infant was transfused several times and seemed to improve slowly. Exact cause of the neonatal difficulty was not determined. It was not due to Rh incompatibility but may have been due to ABO isoimmunization.

Infant was fed a one-half skimmed milk and carbohydrate mixture but did not gain well, had 5 to 6 bulky stools daily and upon discharge from hospital at age of 1 mo., weighed only 2.5 kg.

At age of 5½ wk. she was readmitted because of explosive diarrhea and vomiting leading to severe dehydration. She was given parenteral fluid, blood, and penicillin and then fed a powdered protein milk mixture with a prompt recurrence of the diarrhea on resumption of milk feedings.

At age 2½ mo., after control of repeated attacks of diarrhea by starvation and parenteral alimentation, she was started on a feeding mixture containing a protein hydrolysate, vegetable fats and dextrimaltose (nutramigen®, Mead Johnson and Company) because of possibility that she might have an allergy to cow's milk. Diarrhea was controlled immediately with this synthetic feeding mixture and she began to gain weight slowly. Attempts were subsequently made to add other foods to diet but they always resulted in recurrence of diarrhea. For the following 2 mo. she was fed only nutramigen® and received the following dietary supplements daily:

(1) Crystalline vitamin D 750 u.
(2) Ascorbic acid 66 mg.
(3) Crude liver extract 1 cc. intramuscularly; stopped because of an urticarial reaction after 5 days.

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(4) Unknown amounts of folic acid given parenterally for 2 wk.
(5) Elemental iron 65 mg. in the form of ferrous sulfate.

Infant was discharged from hospital 9 days before admission to Grace-New Haven Community Hospital. During the previous 4 wk. the mother had noted increasing prominence of breasts without evidence of development of any other secondary sex characteristics. For about 2 to 3 wk. she had seen the development of a filmy opaque membrane over the bulbar conjunctivae, and for

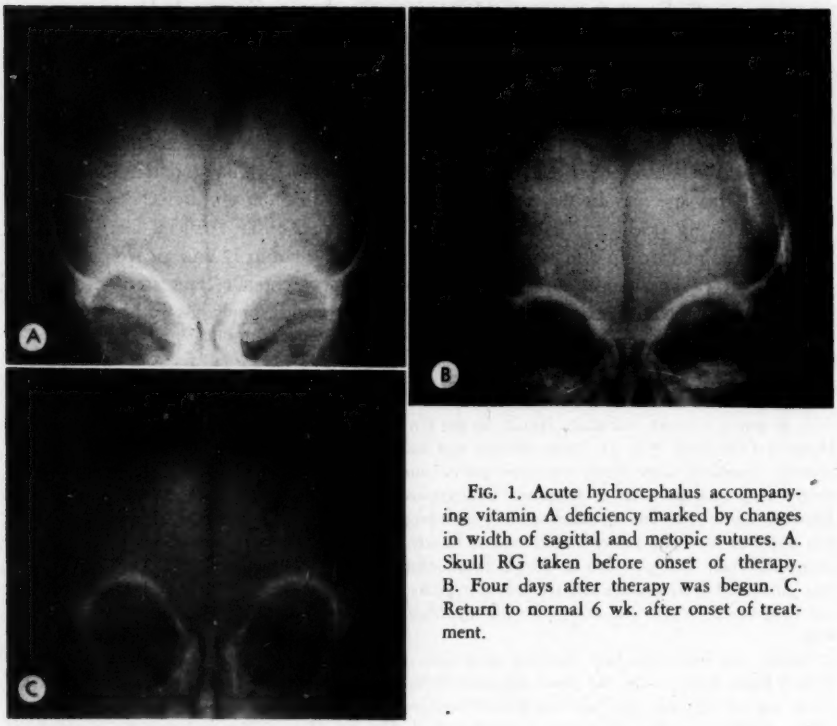

FIG. 1. Acute hydrocephalus accompanying vitamin A deficiency marked by changes in width of sagittal and metopic sutures. A. Skull RG taken before onset of therapy. B. Four days after therapy was begun. C. Return to normal 6 wk. after onset of treatment.

about 1 wk. she had noted asymmetry of face with mouth drawn to one side, as well as increasing frequency of bowel movements.

On specific questioning at the time of admission, the mother stated that the baby did not seem to be as alert as her other children, that she showed no interest in her environment and appeared to be retarded mentally as well as physically.

Physical examination: Patient was a thin, irritable, chronically ill-appearing baby, moderately dehydrated, who followed objects with her eyes but did not lift her head and would not roll over. Weight was 3.7 kg., fontanelle was slightly depressed but head contour was normal. There was facial asymmetry with evidence of a R nuclear 7th cranial nerve injury. The conjunctivae were dry and red with a grayish-white, dry and scaly opaque membrane involving bulbar conjunctivae of both eyes and spreading over the cornea. Eye changes appeared to be characteristic of xerophthalmia. There was marked enlargement of breasts of a firm, glandular rather than adipose nature. Heart and lungs were normal. Liver was palpable 4 cm. below costal margin and spleen palpable 2 cm. below costal margin. Genitalia appeared normal externally and no significant adenopathy was found. All reflexes were physiologic.

Laboratory Findings: Hemogram revealed RBC count 2.8 million/cmm., Hgb. 10.8 gm./100 cc., hematocrit 28%, with WBC count varying from 6 to 16 thousand/cmm. and a normal differential. Reticulocyte count 1.5% of total RBC count. Red blood cell fragility was normal and platelets were present in average numbers on smears of peripheral blood. Coomb's test and tests for presence of cold agglutinins were not remarkable. Bone marrow revealed presence of a normal myeloid series with slight erythroid suppression.

Urine was completely negative as were serologic tests for syphilis. Tests of liver function included a 3+ cephalin flocculation, 0.9% bromsulfalein retention in 45 min. after injection of dye (5 mg./kg. body weight), thymol turbidity 4.6 units, an alkaline phosphatase 17.4 Bodansky units; a total bilirubin 0.48 mg., an albumin of 3.3 and a globulin of 2.1 gm./100 cc.

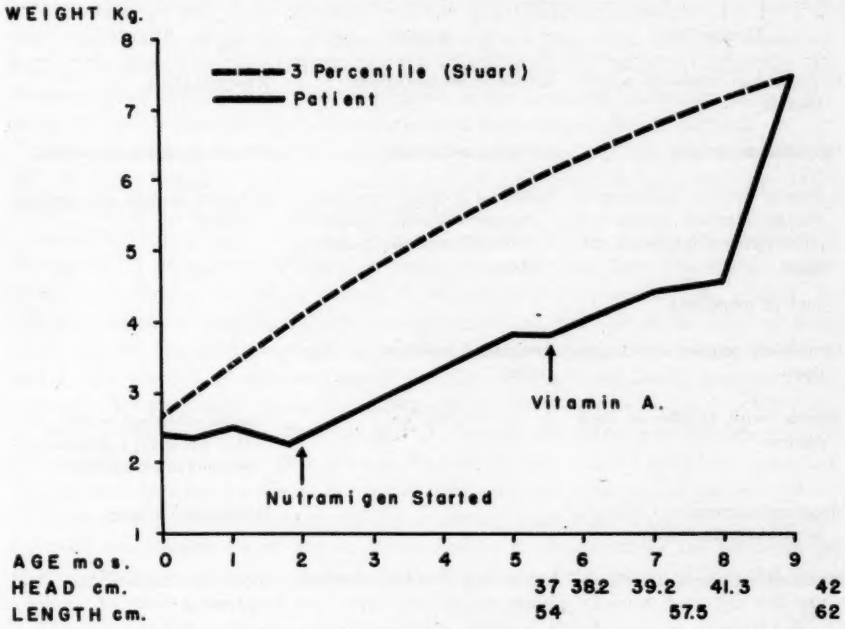

CHART 1. Growth curve demonstrating change in weight, length and head size after vitamin A therapy.

Analyses of serum revealed normal electrolyte concentrations; a galactose tolerance test and epinephrine tolerance test were within normal limits. ECG was normal and radiographs of the chest and abdomen were indeterminate. Culture of stool yielded only E. coli on several occasions and numerous stools in 1-100 dilution digested gelatin. A 4 day stool collection did not contain an excess amount of lipid. EEG was within normal limits. An attempt was made to collect a 24 hr. urine specimen for 17-ketosteroid determination but this was unsuccessful. Papanicolaou stains of vaginal secretions revealed a cornified vaginal mucosa with histologic appearance of vaginal epithelium of an adult female on 18th day of her menstrual cycle. Serum vitamin A concentration was determined by Dr. Augusta McCoord of University of Rochester School of Medicine and was reported to be 40 International U/100 cc.—a value definitely below normal level.

Course: On 3rd hospital day patient was noted to have a bulging fontanelle. Skull radiographs which had previously been normal showed increasing separation of sutures (Fig. 1). Lumbar puncture at this time revealed an increased cerebrospinal fluid pressure (280 mm. H_2O) with a normal protein concentration. Subdural taps bilaterally were negative. At this time she was given intra-

muscularly vitamin A, 100,000 u. daily for 3 days, and thereafter maintained on a multivitamin preparation. By 9th day xerophthalmia had cleared completely, breasts had diminished in size and liver and spleen were no longer considered to be enlarged. Right facial palsy began to disappear on 7th day of therapy and has cleared completely since. Bulging of fontanelle persisted, however, and an increase in head size of 2.2 cm. occurred during the following 4 wk.

Follow-up examinations have revealed a bright, healthy, alert, well-developed baby who has shown a marked increase in growth (chart 1), and is still being maintained on nutramigen® alone

TABLE 1

SIGNS OF VITAMIN A DEFICIENCY

Human Cases	Animals	Patient
Eye changes—xerosis to xerophthalmia	Xerosis to xerophthalmia	Xerophthalmia
Epithelial metaplasia	Epithelial metaplasia	Cornified vaginal epithelium
Failure of growth—degenerative changes of muscle, cessation of proliferation of epiphyseal cartilage	Failure of growth—degenerative changes of muscle, cessation of proliferation of epiphyseal cartilage	Retarded mental and physical growth
Lymphoid hypoplasia		
Diminished resistance to infection	Diminished resistance to infection	
Anemia—with atrophy of bone marrow		Anemia—resistant to iron, folic acid and liver; erythroid suppression in bone marrow
Hepatosplenomegaly—? due to hemosiderin deposition		Hepatosplenomegaly
Increased cerebrospinal fluid pressure	Increased cerebrospinal fluid pressure	Increased cerebrospinal fluid pressure
	Cranial nerve injury	Seventh cranial nerve injury
	Increased sensitivity of end-organs to estrogen effect	Gynecomastia
		Cornified vaginal epithelium

with added supplements of a multivitamin preparation and folic acid. Growth of head is now within normal limits. There is no evidence of physical or mental retardation at present time, 2½ mo. after beginning of a vitamin A therapy.

DISCUSSION

Bloch[1] first described in detail the signs and symptoms of vitamin A deficiency in humans from his studies of Danish children during World War I. In addition, subsequent clinical studies have revealed certain other changes in adults and children[2–4] (table 1). These manifestations include eye changes varying from xerosis to keratomalacia,

as well as epithelial metaplasia of the skin and mucous membranes of the trachea, bronchi, sinuses, pancreatic ducts and gastrointestinal and genitourinary tracts. Failure of growth has been described with degenerative changes of the muscle, consisting of swelling of the muscle fibers, loss of striation, and even complete degeneration, as well as changes in the bones with cessation of the proliferative activity of the epiphyseal cartilage resulting in a narrow band of atrophic cartilage. Lymphoid hypoplasia and anemia with atrophy of the bone marrow and possibly diminished resistance to infection as a result have all been noted. Diarrhea has been reported as a frequent symptom and may result from changes in the mucous membranes of the gastrointestinal tract. Hepatomegaly and splenomegaly have been reported by Sweet and K'ang[4] in approximately 50% of their cases. The pathogenesis of these lesions was not clear with the only consistent finding an increase in hemosiderin deposition. Blackfan and Wolbach[3] described the development of keratomalacia, cellular elements in the urine and hydrocephalus in a 3½ month old infant maintained on a synthetic diet because of an allergic diathesis.

Although many of the changes noted in experimental animals deficient in vitamin A resemble those found in deficient states in man, the findings are generally more widespread than those described in human cases (table 1).

Mellanby,[5,6] in young dogs, and Wolbach and Bessey,[7] in young rats, investigated the relation of vitamin A deficiency to certain neurologic disorders. The former postulated that a certain amount of vitamin A was necessary for normal bone growth. In deficiency states a controlling influence on growth is lost. The size of the bone increases (especially the cancellous bone of the skull) and causes compression of the overlying nerves with pressure necrosis and loss of function. Wolbach and Bessey postulated that neurologic lesions result when a normally growing central nervous system is compressed by bones whose rate of growth is retarded. As a result, the nerve roots herniate through the intervertebral foramina. Both theories attribute the cause of the neurologic signs to a disproportion between the size of the cranial vault and that of the central nervous system. The associated increased cerebrospinal fluid pressure which both groups of investigators observed was thought to be due to interference with absorption of the cerebrospinal fluid. Increase in cerebrospinal fluid pressure has also been produced in cows on a vitamin A-deficient diet[8] and has been reversed on adding vitamin A to the diet.

Both in castrated and noncastrated male rats, vitamin A deficiency increases the sensitivity to estrogen as measured by epithelial metaplasia and changes in the sex organs.[9] Other data[10] indicates that in rats which have a mild vitamin A deficiency the administration of growth hormone fails to stimulate growth but rather results in increased mortality, decreased length of survival, and frequently precipitates acute symptoms of vitamin A deficiency.

In the patient described, the facial palsy and the increased intracranial pressure may possibly be accounted for by the theory of Wolbach and Bessey. The rapid clearing after the institution of massive vitamin A therapy and the absence of any other likely cause make it probable that these signs were due to vitamin A deficiency. The possibility of a thiamine deficiency as a contributing factor in the neurologic disorder was considered unlikely in view of the complete absence of any signs of vitamin B_1 deficiency (cardiac enlargement, anasarca, constipation, oliguria, reflex changes).[12]

The explanation of the hypertrophy of the breasts is not as clear. It is possible, however, that the deficiency of vitamin A sensitized the mammary tissue so that it became hyper-

plastic under the stimulation of a concentration of estrogen which is usually ineffective. Again, the rapid disappearance of the gynecomastia after specific therapy is suggestive evidence as to its etiology.

The reason for the six week interval from onset of vitamin A therapy to great acceleration in weight gain remains obscure.

It is of interest that despite the fact that the infant did not increase her weight rapidly initially, she did show a prompt response in skeletal growth with addition of vitamin A to her diet (chart 1).

As a practical consideration it is worth emphasizing that serious vitamin A deficiency may occur in infants maintained on synthetic diets unless specific vitamin A therapy is included. The signs of vitamin A deficiency in young infants may resemble more closely the findings in experimental animals than would those in older patients. The rapid growth of young infants and laboratory animals may be the reason for this similarity.

Summary

A case of vitamin A deficiency in a 5½ mo. old infant is presented. The multiple manifestations of vitamin A deficiency as noted in this case clearly resemble the signs of deficiency described in experimental animals. The need for adequate supplementation of synthetic diets is re-emphasized.

Acknowledgment

The authors are indebted to Dr. William U. Gardner, Department of Anatomy, Yale University School of Medicine, for his suggestions regarding this patient.

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SPANISH ABSTRACT

Avitaminosis A: Caso de una niña de cinco y medio meses de edad con manifestaciones poco frecuentes

El interés de este caso de avitaminosis A depende de su edad pues la costumbre de la alimentación láctea de origen animal en esa época hace que los signos puedan ser distintos de los niños mas grandes.

Se trata de una niña a término, cuya madre se alimenta adecuadamente durante el embarazo, que se le administró un hidrolisado proteíco, grasas vegetales y dextromaltosa desde los 2½ meses de edad por padecer diarrea probablemente por alergia a la leche de vaca, suplementada con vitaminas D y C en cantidades adecuadas pero no con vitamina A. Al mes y medio de dicha dieta apreció aumento progresivo de los senos de la niña y una semana después la formación de una fina membrana, opaca, en la conjuntiva ocular, y finalmente una semana mas tarde la madre notó asimetría facial con desviación de la comisura bucal hacia un lado y evacuaciones frecuentes. Ademas, parecía estar fisica y mentalmente, retardada para su edad. La exploración física demostró desnutrición algo severa, fontanela deprimida, parálisis nuclear del nervio facial derecho, conjuntivas secas y rojas con una membrana blanco grisasea, seca y descamativa que las cubría totalmente y se extendía sobre la cornea, lesiones que fueron clasificadas como características de xeroftalmía. Tenía también hipertrofia glandular marcada de los senos, hígado palpable a 4 cm. abajo del reborde costal y el bazo a 2; sus órganos genitales externos eran normales y no había desarrollo de otros caracteres sexuales secundarios.

Los resultados de laboratorio comprobaron: anemia marcada, proteínas sanguíneas dentro de límites inferiores normales, presencia de mucosa vaginal cornificada por el método de tinción de Papanicolaou correspondiente a un epitelio vaginal de mujer adulta en el decimo octavo día de su ciclo menstrual y la dosificación de vitamina A en el suero sanguíneo de 40 unidades internacionales por 100 c.c.

En los días siguientes al ingreso al hospital con el cuadro clínico descrito, la fontanela presentó abombamiento y las radiografías de cráneo que habían sido normales mostraron separación de suturas y la presión del líquido cefalorraquídeo aumentó hasta 280 milímetros, momento en el cual se iniciaron 100.000 unidades de vitamina A diarias por vía intramuscular 3 días en total y se continuó con un preparado multivitamínico por vía oral. Nueve días después la xeroftalmía había desaparecido, los senos habían disminuido, y el hígado y bazo no eran palpables, la parálisis facial mejoró y solo el abombamiento de la fontanela persistió y a las 4 semanas la cabeza había aumentado 2.2. cm.

A los 2 ½ meses de iniciada la vitaminoterapia la niña estaba completamente curada, con edad mental y desarrollo físico correspondiente a su edad.

De acuerdo con los experimentos de avitaminosis A en animales, se suguiere que la hidrocefalia y la parálisis facial sean producidas por una desproporción entre el tamaño de la bóveda craneana y el del sistema nervioso central y el aumento de presión del líquido cefalorraquídeo a una interferencia en su absorción.

En cuanto a la hipertrofia mamaria es posible que una deficiencia de vitamina A sensibilice el tejido mamario y la acción de estrógenos en cantidades usualmente indiferentes determine su hipertrofia.

La rápida respuesta de estos síntomas a la vitamina A no deja lugar a duda acerca de su etiología avitaminósica.

La conclusión práctica es no olvidar nunca administrar vitamina A simultaneamente con las otras variedades de vitaminas.

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GALACTOSEMIA

Report of Case with Autopsy

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TO DATE 21* cases of galactosemia have been reported since the initial report of the syndrome by von Reuss[1] in 1908. Over half of these cases have been reported within the last 7 years. The cardinal features of this syndrome are galactosuria, galactosemia, albuminuria, malnutrition as evidenced by failure to gain weight while being maintained on normal or high caloric intake, hepatomegaly and frequently, mental retardation and cataracts. A familial tendency may be manifested. Commonly the serum bilirubin is elevated and may or may not be accompanied by jaundice. In recent months the literature on this disease has been reviewed by Bell and associates.[2, 3]

CASE REPORT

D. H., a 2 mo. old white female, was born of a normal pregnancy and delivery. Birth weight was approximately 2.7 kg. Dietary history previous to 3 wk. of age is uncertain. There was no history of familial disease. The parents and 7 siblings are living and well.

The baby was first seen by the foster mother at 3 wk. of age at which time multiple boils were present which were treated with parenteral penicillin, incision and drainage. At this time the baby was severely emaciated, weighing less than at birth. Shortly after this, the stools were diarrheal and the carbohydrate was changed from karo to dextri-maltose with improvement. From 3 wk. of age, in spite of a known adequate caloric intake and in the absence of regurgitation and diarrhea, the baby continued to show no improvement of the previously described emaciation. During this time the weight gain was gradual to 3.7 kg. at time of admission to the hospital. However, this gain in weight was found to be due to accumulation of fluid in the abdomen.

Physical examination revealed a poorly developed, pale and severely emaciated white female infant with marked distention of the abdomen. The baby appeared acutely and chronically ill with respiratory distress. There was marked prominence of the abdomen with venous distention and evidence of ascitic fluid. The consulting ophthalmologist found normal retinae and lenses. Paracentesis resulted in more than 300 cc. of clear, yellow fluid. Following this procedure, the liver was readily palpable 5 cm. below the costal margin and was noted to be very firm with a sharp edge. The spleen was barely palpable.

Laboratory data: Hgb. 11.2 gm./100 cc.; RBC 3.5 million/cmm.; WBC 10 thousand/cmm. with polymorphonuclears 49%, lymphocytes 45%, monocytes 4% and basophiles 2%. Urinalysis revealed a proteinuria of 2+ and a 3+ reaction to Benedict's solution, which was confirmed on a subsequent examination. Kahn flocculation test was negative; fasting blood sugar 164 mg./100 cc.; NPN 31 mg./100 cc.; total protein 6.4 gm./100 cc. with an albumin of 3.9 gm./100 cc. and globulin of 2.5 gm./100 cc. Stool examination revealed the presence of a normal quantity of neutral fat and absence of starch granules. The examination for trypsin was unsatisfactory. Liver studies resulted in a total serum bilirubin of 4.4 mg./100 cc. of which 4.3 mg./100 cc. gave a direct reac-

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* Since this report was prepared, an article on Galactosemia and Its Relation to Laennec's Cirrhosis, by Townsend, E. H., Mason, H. H., and Strong, P. S., appeared in PEDIATRICS 7:6, 1951. Five additional cases were reported.

tion. Bromsulphalein retention was 22% after 80 min. Thymol turbidity was 3 units and the cephalin flocculation 3 +. The reducing substance in the urine was proved to be galactose by fermentation, mucic acid and osazone tests. Oral glucose tolerance test using 1.5 gm. glucose/kg. resulted in the following total blood sugar determinations: fasting—170 mg./100 cc.; ½ hr.—216 mg./100 cc.; 1 hr.—315 mg./100 cc.; 2 hr.—384 mg./100 cc.; 3 hr.—295 mg./100 cc. (chart 1).

On the 6th hospital day, shortly after the diagnosis of galactosemia was established, the baby suddenly and unexpectedly died. Immediate postmortem blood sugar revealed a total blood sugar of 250 mg./100 cc. of which 200 mg./100 cc. was nonfermentable.

Pathologic report: The examination was performed 1 hr. after death, the body having been re-

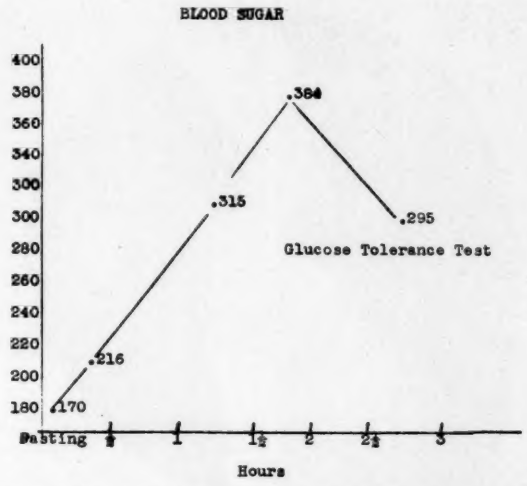

CHART 1. Glucose tolerance curve. At end of 2¾ hr. there remained 295 mg. sugar/100 cc. blood.

moved promptly to the refrigerators. The appearance was that of a white female infant weighing 3.0 kg. and obviously undernourished. Cataracts were not demonstrated, nor was an icteric tinge to the sclerae seen. The lungs appeared crepitant throughout, except for the posterior portions which presented increased consistency suggestive of hypostatic pneumonia.

On opening the abdomen it was noted that approximately 60 cc. of clear straw-colored fluid escaped. The liver extended about 3 cm. below the costal margin and weighed 150 gm. It presented a greenish color, which after being in formalin for several hours became marked. The liver capsule was thin and dipped down between tiny nodules 1 to 3 mm. in diameter (Fig. 1). On cut section it was noted that the nodules were fairly evenly dispersed throughout the organ. With a magnifying glass it was clear that the nodules were sharply delineated and separated by translucent connective tissue. Three larger circumscribed nodules (adenomata), measuring 2, 1.5 and 1 cm. in widest diameter, were seen. They stood out as pale nodules against the greenish background of the remainder of the liver, after fixation. Microscopically, these later proved to be composed of glycogen-laden cells (see below). The spleen weighed 90 gm. The capsule was not unusual and on cut section, the Malpighian corpuscles were indistinct. The red pulp was prominent and the trabeculae thickened (Fig. 1). The gall bladder contained approximately 1 cc. of thick, viscid bile. The mucosa and wall were not unusual. Bile identical in appearance to that in the gall bladder was demonstrated in the extrahepatic ducts. After fixation, the extrahepatic and first portion of the intrahepatic biliary duct system was cut transversely at 1 to 2 mm. intervals to determine the presence or absence of obstruction to the bile flow. None was found.

Histologic examination was performed on tissues in formol-Zenker's solution and 10% neutral-

ized formalin. In addition, thin 4 mm. sections of liver, spleen, adrenal and pancreas were fixed in Bouin's solution and absolute alcohol. The histologic appearance of the liver revealed the presence of lesions suggestive in some areas of biliary cirrhosis. The organ contained numerous small nodules, rather evenly dispersed throughout. The nodules were separated by thin strands of condensed connective tissue which contained many proliferating bile ducts and ductules (Figs. 2 and 3). The 3 isolated, large nodules mentioned above in the gross description were composed almost entirely of enormous, glycogen-infiltrated cells. The liver nuclei were often large and hyperchromatic with prominent nucleoli. Mitotic figures were not noted. The cytoplasm of the liver cells was voluminous and often finely granular. The cells appeared to contain very little bile pigment. The

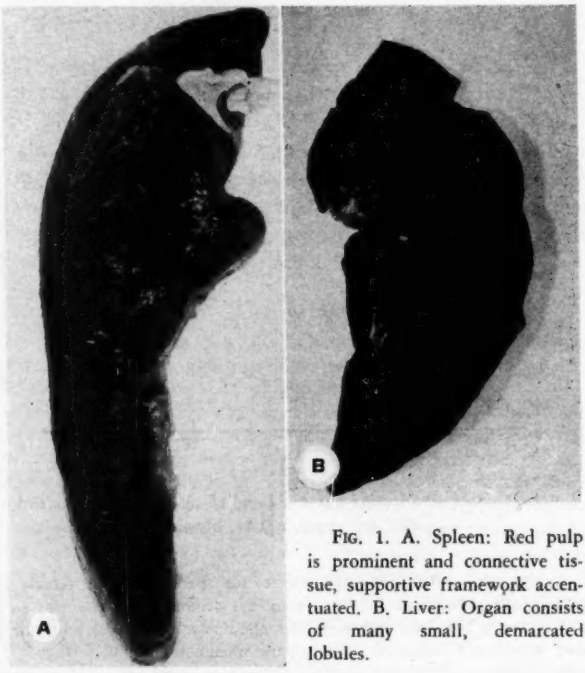

FIG. 1. A. Spleen: Red pulp is prominent and connective tissue, supportive framework accentuated. B. Liver: Organ consists of many small, demarcated lobules.

cells frequently assumed a tubular or alveolar pattern (Fig. 4). Bile canaliculi were distended with bile "thrombi" or casts. Very little bile appeared in the bile ducts in the portal areas, and the latter, while in a proliferative state, were not dilated. Sections from absolute alcohol fixation treated by periodic acid—Schiff's reagent method—showed fine granules in the cells containing abundant glycogen. The remainder of the liver cells were extremely "glycogen poor." Very tiny sudanophilic droplets were found in approximately 80% of the liver cells. Perl's iron stain was faintly positive, and this was restricted likewise to the glycogen-laden cells. Acid-fast stains were negative, thus ruling out the presence of ceroid pigment. There was no microscopic evidence of osteitis fibrosa. Some fatty infiltration of the heart was noted. Histologic examination of the remaining organs was not abnormal.

The postmortem chemical examination of the liver was performed. Twenty-five grams of liver was placed in a deep freeze within 10 min. from the start of the autopsy. Analysis of 2 liver samples of about 2 gm. each failed to show any glycogen by a method which is routinely used to measure 0.1% glycogen with a precision of about 5%. We can conclude that there was much less than 0.05% glycogen, the normal being 1.4%. Analysis for total lipid content of the same 2 samples was 6.4% each. This is a figure slightly higher than normal.

Anatomic diagnosis: Cirrhosis of liver; congestive splenomegaly (early Banti's spleen); lipoid pneumonia; ascites and fatty infiltration of heart.

Discussion

Liver Lesion: Of the 21 cases of galactosemia described to date, four have been studied at autopsy and one on biopsy material. The first case reported by von Reuss[1] in 1908 showed the liver to be enlarged and containing numerous fine nodules. The

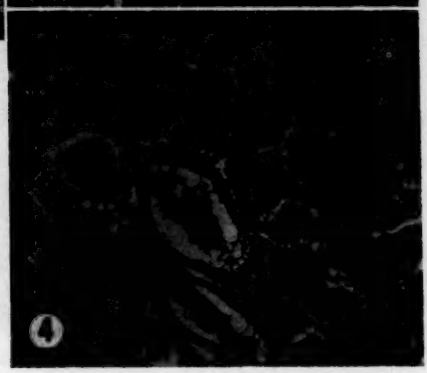

Fig. 2. Fine connective tissue septa separate liver lobules. Portal areas are regularly arranged. Peculiar acinar structures contain bile thrombi.

Fig. 3. Proliferating bile ductules are present. Liver sinusoids are wide and empty. Liver cells are vacuolated.

Fig. 4. Large acinar structures containing bilirubin casts are prominent in liver.

picture was considered compatible with portal cirrhosis. The nature of the structure of the liver in the case cited by Goodwin[4] is not clear. The two cases described by Bell[2] and co-workers represented fatty infiltration of the liver and fatty cirrhosis. The morphology of the liver in the case described by Donnell and Lann[5] was similar to that of Bell and associates. The histologic appearance of the liver lesion in this case is not compatible with the classical type of lesion seen in biliary or Laennec's cirrhosis. The presence of the "gland-like structures," accompanied by the adenomata, place it in a separate category. Bile "thrombi" were so numerous and large that they may have played an obstructive role. The cause of the obstruction may be an abnormal type of bile, leading to inspissation in the bile canaliculi. The case presented revealed an increased total serum bilirubin of which almost all gave the direct reaction and this supports the hypothesis of an obstructive nature of the liver lesion.

Glycogen: The amount of glycogen found at autopsy depends on antemortem body

temperature, postmortem environmental temperature, body activity and glycogen intake. These factors were optimal for a satisfactory glycogen estimation. By means of special stains (Best's carmine; periodic acid-Schiff reagent) with control sections, glycogen granules were found exceedingly sparse. They were limited to the large cells (Figs. 5A and B). This finding is in accordance with the chemical determination of gross liver which revealed insignificant amounts of glycogen.

In diabetes mellitus, the liver frequently shows intranuclear glycogen. In a lesser number of these patients glycogen is found in the renal tubules. Glycogen in these locations has not been mentioned in the cases of galactose diabetes reported, nor was it seen in

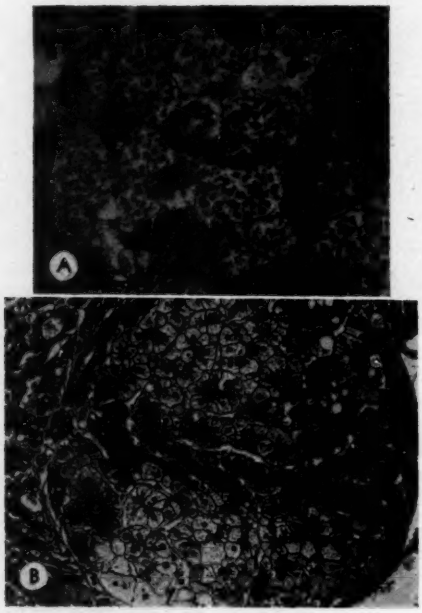

FIG. 5. A. Periodic acid-Schiff positive granules (probably glycogen) are present in large "blown-up" liver cells. B. Liver: Nodule containing large polygonal clear glycogen-containing cells.

the present case. In this respect, the amount of glycogen in this case differs from the second case reported by Bell and co-workers.[2] They demonstrated that the liver contained an amount of glycogen which fell within normal limits. It would appear clear from the two cases of these workers and the present case that the nature of the hepatic disorder does not involve the presence of abnormal or excessive glycogen in the hepatic cells, as has been proposed.[6]

Sudanophilic Material (Lipid): Sudan stains revealed sudanophilic droplets in the liver cells. The droplets were fine and small for the most part. Scattered areas were seen where the entire liver cell cytoplasm was occupied by a vacuole (Fig. 6). The significant amount of lipid in the liver cytoplasm deserves special mention. A number of possibilities exist as to its pathogenesis. The infant during the first weeks of life was in a state of malnutrition. This implies inadequate lipotropic factors with resultant accumulation of

fat in the liver. Possibly galactose in excess in the blood may interfere with the utilization of lipotropic factors by means of unrecognized enzyme systems. Fat in the liver in diabetes mellitus and cystic fibrosis of the pancreas is at present an unexplained phenomenon. Liver cell damage results in inability to utilize the lipid brought to it from the fat storage depots, and hence its accumulation in the cell. As the liver cell damage was spotty, so was the fatty infiltration. Sudanophilic material may rapidly disappear from the liver cell under optimal dietary conditions, that is, a diet rich in protein and carbohydrate. This would explain the decrease in liver size upon removing galactose from the diet in galactose diabetes.

Hepatomegaly: A number of the cases of galactose diabetes reported in the literature were characterized by hepatomegaly.[1, 2, 6–9] Following the clinical diagnosis milk was withdrawn from the diet and the patient gained weight, symptoms regressed and the hepatomegaly subsided. The rapid change in the size of the liver was, in these cases, most probably due to reduction in the amount of lipid content. One visualizes these livers as

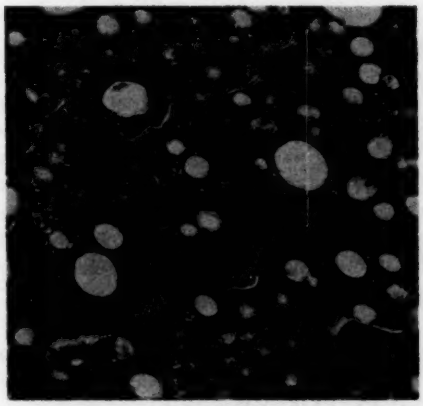

FIG. 6. Liver: Large vacuoles have completely displaced liver cell cytoplasm.

being the "seat" of fatty infiltration. Whether the fat in the liver preceded the disturbance in galactose metabolism is a matter for speculation. The infant described by von Reuss manifestated an alcoholic history, extending throughout the whole life span of eight months. In the case reported here there was no way of knowing whether the fatty infiltration of the liver preceded or followed the development of galactosemia. The liver lesions of the cases of Bell manifestated fatty infiltration. In his first case this was extremely marked with almost every cell engorged with fat.

A second mechanism to explain the hepatomegaly has been proposed by Norman and Fashena[10] as well as Mason and Turner.[11] They suggested the following theory: "Since the body cannot metabolize galactose, this sugar accumulates in the blood and causes a depression of blood glucose. The high blood galactose level 'deceives' the regulators of blood sugar and causes an excessive conversion of glucose to glycogen, which causes hepatomegaly and hepatic dysfunction. When lactose, the source of galactose, is withdrawn from the diet, normal glycogen-glucose equilibrium is re-established and the liver returns to normal."

This mechanism may explain the hepatomegaly in the reports of cases by these authors,

but certainly in the second case of Bell and co-workers,[2,3] as well as the present case, glycogen was not shown to be increased in amount, either chemically or histologically. The appreciable enlargement of the liver in the two cases of Bell and one autopsied case of Donnell and Lann[5] apparently were due to fatty infiltration. If we believe that the primary disturbance in this syndrome is an inborn defect of galactose metabolism, then the liver damage may depend on one or more of the following factors:

1. Excess glycogen in the liver cell.
2. Toxic effect of high galactose concentration.
3. Low glucose concentration.
4. Fatty infiltration of liver cells.

The first theory, namely, liver cell damage from glycogen accumulation in the cytoplasm hardly appears tenable. In von Gierke's disease liver degeneration or necrosis is not evident. Insoluble or colloidal glycogen may almost completely displace the nucleus of the liver cell in a variety of conditions, including diabetes mellitus where evidence of nuclear degeneration is absent. Furthermore, as pointed out by Mellinkoff,[12] ordinarily the deposition of glycogen in the liver tends to protect the organ.

The second theory, proposing a damaging action of galactose on the liver cell, has been put forward by Mellinkoff.[12] There seems to be no reference in the literature incriminating galactose as a hepatic toxic agent. The present investigators attempted to damage rabbit livers by feeding and injecting large amounts of galactose. Eight albino rabbits, weighing approximately 2 kg. each, were used in the experiment. The first four were injected intravenously daily for 21 days with 20 cc. of 25% galactose in distilled water. In addition, the drinking water was a saturated solution of galactose. Twenty grams of galactose were added to the daily food pan. The second four animals were treated in the same way using glucose instead of galactose. It is realized, of course, that the daily or total intake cannot be ascertained accurately by this method, for no attempt was made to determine blood levels or urinary levels of glucose or galactose. All eight animals were killed on the 21st day and complete autopsies were immediately performed, the tissues being fixed in Zenker's and absolute alcohol.

The liver sections of both the galactose and glucose animals revealed the presence of abundant histologically demonstrable glycogen, the periodic acid-Schiff reagent being used as stain. The glycogen disappeared after the saliva test. The amount of glycogen in the galactose animals was approximately one third more than in the glucose animals. No evidence of liver damage was ascertained. Fat stains of the liver and kidneys failed to show the presence of this substance.

The third theory, that of low glucose level causing liver and kidney damage, was proposed by Norman and Fashena.[10] This likewise seems unfounded because in hyperinsulinism no lesions of these organs are noted. Furthermore, the changes in the liver in malnutrition and starvation are not due directly to a low glucose level, but rather to absence of the lipotropic factors in the diet.

The fourth theory of the cause of the liver damage, that is by fatty infiltration, was proposed by Bell and co-workers.[2,3] Certainly in their cases the fatty infiltration was extreme and one case showed early cirrhosis. Thus, the role of the fatty infiltration is suggested.

Three mechanisms are possible in the light of present knowledge:

1. Idiopathic disturbance in galactose metabolism leading to excessive fat and glycogen deposition in the liver through disturbed enzyme systems.

2. Congenital fatty cirrhosis or malformation of the liver resulting in disturbed carbohydrate metabolism.

3. Congenital disturbance in bile excretion leading to liver cell damage and resulting in galactosemia and galactosuria.

Summary

A case of proved galactosemia in a two month old female infant with necropsy findings has been reported. The liver lesion in this case does not clearly fit into the category of Laennec's cirrhosis or biliary cirrhosis. The presence of the adenomata, rich in glycogen, and the peculiar acinar structures separates it into a distinctive type of lesion. It is proposed that these cases represent congenital and familial cirrhosis.

The administration of large amounts of galactose to rabbits failed to produce liver cell degeneration or necrosis. As suggested from the cases reported in the literature and in view of the lack of agreement on the pathogenesis among observers, the same mechanism may not be responsible for all of the cases of galactose diabetes recorded.

Acknowledgment

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Spanish Abstract

Galactemia con Cirrosis del Higado

Se presenta un caso de galactosemia en un niño de 3 meses en el que los datos principales de la autopsia fueron los de cirrosis hepática con formaciones de los acinos conteniendo trombos de bilis y los de esplenomegalia congestiva.

Se plantea la posibilidad de que haya casos en que el trastorno del metabolismo de la galactosa sea primario y otros en que sea secundario a una cirrosis hepática congénita o adquirida. La galactosa administrada a conejos no produjo lesiones en la autopsia. Se discute la etiología y patogenia del síndrome.

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PROGNOSIS FOR SURVIVAL IN THE LEUKEMIAS OF CHILDHOOD

Review of the Literature and the Proposal of a Simple Method of Reporting Survival Data for These Diseases

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THE best therapy for a patient with a fatal neoplastic disease must be based upon considerations of the immediate clinical condition of the patient, upon the natural history of the disease and upon the value of all the therapeutic means that may be able to affect the course of the disease and its clinical manifestations in the patient. In the evaluation of the efficacy of a particular type of therapy, it is important to separate, when possible, the effects of a particular type of treatment on the clinical manifestations of the disease in the patient from its effects on the ultimate results of the disease.

In the absence of a definitive cure for neoplastic disease, the application of those measures that will improve the clinical status of the patient is properly a primary concern of the physician. To evaluate such clinical improvement, we can measure the time spent at usual activities appropriate to the age and sex of the patient, reduction in hospitalization, time free from pain, "remissions" and other clinical criteria.

To evaluate the effects of therapy against the fundamental disease process, the most objective criterion is the increase in survival time resulting from the therapy used. In this review, survival time is necessarily measured from the onset of first definitive clinical symptoms referable to leukemia.

This review has two purposes. The first is to provide the physician with a basis for estimating the total duration of illness of the child. The second purpose is to provide a base line from which the effects of antifolic acid compounds, ACTH, cortisone and other new therapeutic drugs can be compared. There are numerous excellent review articles of the clinical manifestations of leukemia, but they will not be discussed here.

The articles that are reviewed cover the period before the use of antifolic acid drugs and newer compounds. No comparable review of the effects of antifolic acid compounds, ACTH or cortisone could be completed from data available at the time of this review.

The average time of survival of the patient with leukemia, from onset of symptoms, is a frequently quoted figure in the literature. Reference to chart 1A shows that a "normal" curve is a poor fit of the actual distribution of times of survival for this group of patients with leukemia. For data so markedly skewed, an average represents neither the most probable event nor the midpoint of the series. Furthermore, the standard error of an average

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of such data is of limited validity so that the significance of differences of averages cannot be properly evaluated. For these reasons averages are not used in the compilation of statistics in this review.*

The clinical experience with leukemia in particular, and neoplastic diseases in general, provides intuitive support for the type of distribution shown in chart 1B. The asymmetry of this curve is a graphic representation of the familiar clinical observation that the majority of patients with malignant diseases of many forms die relatively soon after the onset of the disease, but a few patients live much longer than this majority, thus making prognosis based on "averages" misleading.

Boag[2] has shown that the logarithms of the survival times, after therapy, of patients

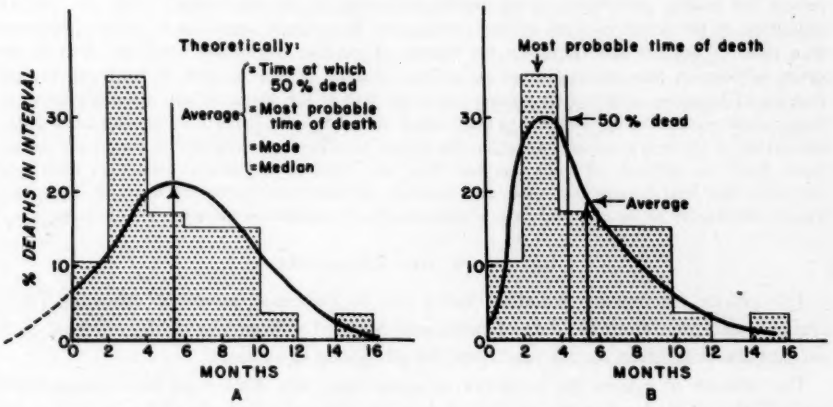

CHART 1. Comparison of application of "Gaussian" or "normal" distribution (A) with "log-normal" distribution (B) to data on survival of 59 children with lymphocytic leukemia.[31] Dotted areas indicate deaths in interval from actual data; solid lines represent calculated distribution. In A, normal distribution has been calculated from average and approximate standard deviation of data. Note considerable discrepancy between actual data and theoretic curve implied by calculation and use of averages, and contrast this with better fit of these same data by distribution B.

with several types of malignant diseases are "normally" distributed. As will be seen later, the survival times for patients with acute leukemias are similarly distributed. Best, Limarzi, and Poncher[3] have analyzed their survival data in acute and chronic leukemias with the aid of a logarithmic time scale, but the details are lacking.

METHODS

Survival times of patients with malignant diseases can be easily assembled by the use of "log-probability" paper with a minimum of calculation† and no detailed mathematical knowledge.[4] The line drawn through the mean of the points so obtained smooths the data and estimates the "true population" of which the patients treated are a small and, presumably, random sample. The

* The mathematically inclined reader can obtain a discussion of the direct handling of such distributions from a paper by Finney,[1] but such computations appear to be complex.

† Calculations:

a. Prepare a table with rows (zones) for 0-1 mo., 1.1-2.0 mo., etc., in ascending order. These zones form column 1.

(Footnote continued on page 50)

logarithmic mean and standard deviations of the series are read by inspection from the chart and, by substituting logarithms for times in months, the standard deviation of the mean (standard error) and the significance of differences between this and the mean of another similar series can be calculated quickly by the usual formulae.

The time required for 50% of the cases of any one series of patients to die is given as being most representative of each series. The range of survival times for the central two-thirds (actually ± one standard deviation of the series) of each group is given. Since the groups of patients studied by the different investigators varied in composition not only as to type of leukemia but also as to age of the patients as well as to the time intervals over which the data were collected, where necessary, a brief summary of such information will follow for each investigator reviewed.

This simple technic can be applied only to series of patients in which all are dead. Berkson and Gage[6] have presented an excellent discussion of a simple, actuarial method of calculating the final results of series composed of both living and dead patients. Boag[2] has given a much more elegant technic for making predictions of the fraction surviving at any stated time, which also permits estimation of the errors involved in such predictions. His technics appear to be more complicated than those of Berkson and Gage, but the expense of calculation probably would be offset by the saving of research time resulting from an earlier evaluation of new methods of treatment. For the problem of leukemia, in which all patients either are dead of the disease or will ultimately die of it, Boag's more general theory simplifies to the problem solved by Lea.[6] Using Lea's formulae and tables, calculation of the results of an incomplete log-normal distribution is a matter of only a few hours' work. Since the methods of both Lea and Boag are based upon Fisher's "maximum likelihood method,"[7] the final logarithmic mean and standard deviation will represent the best fit of this type of distribution to the observed data, whether or not the patients in the series are all dead.

Review of the Literature

The precise fraction of pediatric deaths due to leukemia cannot be estimated from available data, but from the data of Sacks and Seeman[8] it would be of the order of 11.3 per 100,000 population for the year 1940, for all ages up to 14 years.

The relation of age to the incidence of death from this disease has been comprehensively reviewed by Cooke.[9] These data show a log-normal distribution of mortality, with 50% dead by 4.5 years, the central two-thirds of all cases falling between 2.1 and 9.8 years.

The precise influence of heredity on the familial incidence, the type of leukemia or the survival time remains obscure, but the interested reader is referred to the reports of Anderson[10] and Videbaek.[11]

A review of survival times in acute leukemias is complicated by several factors. The incidence and duration of spontaneous remissions in this disease may profoundly influence the data for any very small series. Differentiation as to acute, subacute or chronic leukemia has not always been made, although standard criteria for making such distinctions are now available.[12]

The difficulties of unquestionable identification of the cell series involved in acute leukemias are well known. Diamond[13] has stated that the incidence of granulocytic leukemia in childhood approaches that of lymphocytic leukemia. No comprehensive survey

b. Enter number of patients dying in each time interval opposite each zone, as column 2.

c. Cumulate each row to obtain total number dead by 1 mo., 2 mo., etc. Enter these cumulative totals opposite each zone, as column 3.

d. Calculate the percentage of the total series represented by each cumulative total in column 3; enter as column 4.

e. Plot the cumulative percentages opposite the end of each zone, i.e., at 1 mo., 2 mo., etc., on "log-probability" paper, such as No. 3128, Codex Book Co., Norwood, Mass.

of the relative incidence of leukemia according to cell types involved could be found, but the available information from the literature surveyed for survival statistics is summarized in table 1. The variability shown by these data probably reflects the differences in criteria for classification used by different investigators. As a working estimate, it may be assumed that acute lymphocytic leukemia comprises 70 to 80% of all childhood leukemias, acute granulocytic leukemia up to 20%, unclassified to 10%, acute monocytic leukemia less than 5% and all chronic leukemias not over 2%.

TABLE 1

INCIDENCE OF VARIOUS TYPES OF LEUKEMIA IN CHILDHOOD AS REPORTED BY AUTHORS SURVEYED IN THIS REVIEW

Author		Acute				Chronic		
		Lympho-cytic	Granulo-cytic	Mono-cytic	Unclassified	Lympho-cytic	Granulo-cytic	Mono-cytic
Craver[19]		10	—	—	—	—	—	—
Moody and Davis[20]		42	3	1	2	—	—	—
Ramsay[26]		70	19	—	11	—	—	—
Cooke[27]		50	—	—	2	—	3	—
Dale[29]		46	22	1	—	1	2	—
Sullivan et al.[30]		21	8	1	34	—	1	—
Bierman et al.[31]		90	10	3	—	Not distinguished		
Booth and Rembolt[32]		31	2	2	2	—	3	—
Totals	493	360	64	8	51	1	9	—
%	100	73	13	2	10	—	2	—

Most investigators agree that chronic leukemias are uncommon in children and usually are of the granulocytic type. Keith,[14] Morris and Hurwitz,[15] and Osgood[16] review this disease and present appropriate case histories.

Holowach[17] surveyed the literature on chronic lymphocytic leukemia in children. Falkenstein and Fowler,[18] Craver,[19] and Moody and Davis[20] report cases of lymphocytic leukemia with a duration of 1 to 2 years. Some investigators believe that a true chronic lymphocytic leukemia of childhood equivalent to the adult disease does not exist and that cases of long duration occasionally observed in this disease simply represent the unusual but predictable case. It can be seen by inspection of the various figures (charts 2 and 3) for the duration of patients with leukemia that for some series there is predicated approximately a 1% chance that a case of childhood leukemia may survive 2 years or more.

Diamond[21] has pointed out that 10% of "untreated" patients with acute leukemia may show spontaneous remissions of symptoms of days to weeks. Southam and co-workers[22] found an incidence of 8.7% partial or complete remissions of 3 to 16 weeks in a study of 173 patients, adults and children, with acute leukemia. Zuelzer[23] pointed out the occurrence of more frequent remissions in aleukemic leukemias.

Thus, it is likely that no great error in prognosis estimation will result by using the log-normal distribution method of analysis if all leukemias of childhood—acute, subacute and chronic; lymphocytic, granulocytic and monocytic—are combined for purposes

of analysis of "base-line data." In view of the prospect of early development of cell-specific, chemotherapeutic agents, it does seem imperative that every attempt be made to differentiate such diseases in the future.

Analysis of Survival Data

One of the earliest studies on acute lymphocytic leukemia is the brief data included in the classical article by Minot and Isaacs.[24] This covered 57 cases of acute leukemia observed for an undefined period before the publication of that paper in 1924. Over

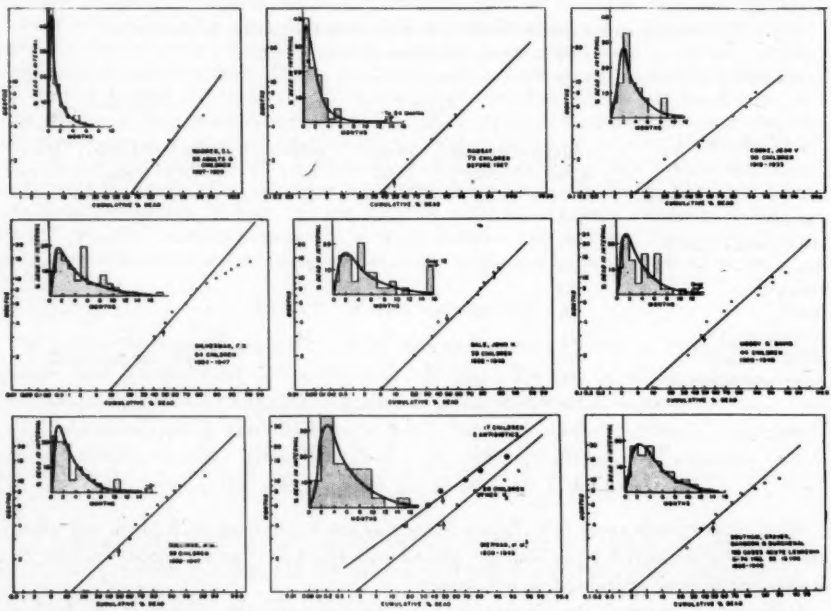

Chart 2. Survival in leukemia of childhood as reported by various authors over periods shown. See text and table 2 for details of cell types involved, stage of disease and treatment used.

50% of these patients were dead in less than two months. Reference to their chart of the age distribution of the cases studied shows that only about 40% of the cases included were in the age group below 15 years; hence, this group cannot be considered typical of the pediatric age group.

The series reported by Warren[25] covered the period 1917 to 1929 and included 85 reported cases in the literature, to which have been added 28 cases of his own. All types of acute leukemia were included. Again, these included both adult and childhood leukemias. Eighty-four per cent of the cases died within six weeks, 18.5% within two weeks. The complete distribution for this group of patients and for the other series analyzed are given in chart 2 and summarized in table 2.

The earliest pediatric review from which survival data could be computed is that of Ramsay,[26] who in 1927 summarized clinical and survival data on 92 cases of leukemia

from the literature and added eight of his own. It is interesting that the group of 12 cases of granulocytic leukemia of known survival have a significantly (5% level) longer survival than those with lymphocytic leukemia. The segregation of 11 "lymphoidocytic" (blast) leukemias from both lymphocytic and granulocytic groups, however, casts some doubt on the validity of this difference. For the entire group of 73 patients on whom survival data were given, the first 50% were dead in about 1.3 months.

Another early study on leukemia in the pediatric age group is that of Cooke,[27] which covers the period of 1918 to 1933. The detailed treatment given these children was not

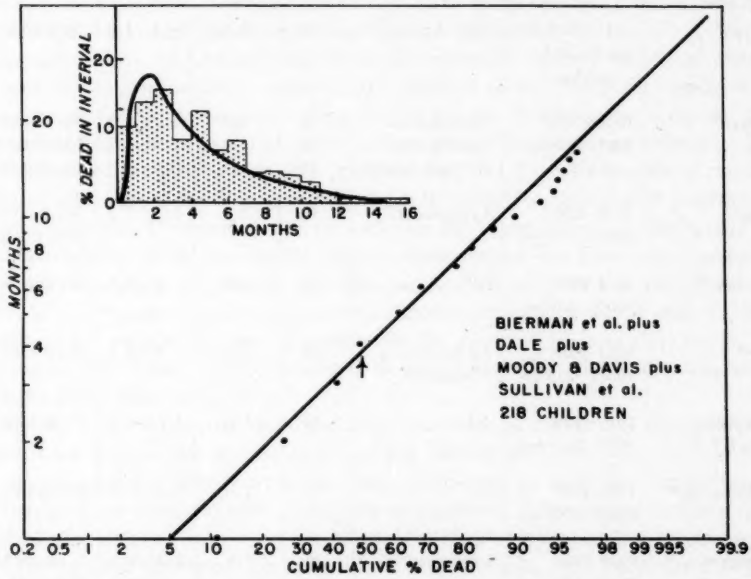

CHART 3. Best estimate of prognosis for survival in leukemias of childhood, based upon combined data of authors noted.[26, 29–31] Treatment for some patients included antibiotics, but not antifolic acid compounds, ACTH or cortisone.

stated, but blood transfusions and/or irradiation were used in at least some of the cases reported. Fifty-four per cent of the patients studied were dead in three months or less. The author felt that the one-eighth of the cases that survived between 6 and 9 months did not represent cases of chronic leukemia, but that "in a small proportion of children with acute leukemia the disease may have a moderately prolonged course."

Silverman[28] reviewed all the cases of leukemia admitted to Babies Hospital, New York, in the period 1924 to 1937. His data did not include all cases of leukemia diagnosed at the hospital. Details of treatment were not given. Fifty per cent of the 64 cases in which the survival after the onset of clinical symptoms was accurately known were dead at 3.6 months.

Dale[29] reviewed a series of 72 cases of leukemia in children 13 years of age and less for the years 1932 to 1948. Survival statistics were presented for only 39 of these pa-

TABLE 2

SUMMARY OF SURVIVAL STATISTICS FOR CHILDREN WITH ACUTE LEUKEMIA

Author	Period Covered and Ages	Types of Leukemia	No. Cases	Mo. to Death for 1st 50%	Central ⅔ Live Mo.	Type of Therapy
Minot and Isaacs[24]	Before 1924 40% <15 yr.	Lymphocytic	57	<2.0		No details
Warren[25]	1917–1929 Adults and children	All	113	0.6	0.2– 1.8	No details
Ramsay[26]	Before 1927 100% <8 yr.	Lymphocytic	56	1.5	0.7– 3.3	No details
		Granulocytic	12	2.0	1.0– 4.3	No details
		All (incl. blasts)	73	1.3	0.6– 3.0	No details
Cooke[27]	1918–1933 100% <15 yr.	Lymphocytic	50	1.9	1.5– 5.5	No details Blood or x-ray
Silverman[28]	1924–1927 100% <13 yr.	All	64	3.6	1.4– 9.0	No details
Dale[29]	1932–1948 100% <14 yr.	All (approx. ⅓ myeloid)	39	4.0	1.8– 8.8	No details
Moody and Davis[20]	1928–1949 100% 15 or less	All	44	3.0	1.5– 6.1	No details
Sullivan et al.[30]	1938–1947 100% <13 yr.	All	59	2.6	1.2– 5.5	No details
Bierman et al.[31]	1939–1948 Under 15 yr.	Lymphocytic	59	4.5	2.3– 8.6	X-ray or blood No antibiotics
		Lymphocytic	17	7.4	4.2–13.0	Blood plus antibiotics
The preceding 4 series combined			218	3.8	1.8– 8.2	
Southam et al.[22]	1926–1948 0–74 yr. 35% <15 yr.	All	150	4.5	2.2– 8.4	Varied, blood antibiotics, x-ray, P^{32}, HN2, etc.

tients and the distinction was not made as to the cell types of leukemia represented by the group. Included in the group were four patients whose survival exceeded 12 months and may include the "chronic" cases of the original group. Treatment was not given. Fifty per cent of the patients represented died within four months of the date of onset of clinical symptoms of the disease.

Moody and Davis[20] summarized the incidence and clinical findings in a series of 48

children, 15 years of age and less, with leukemia admitted to Strong Memorial and Rochester Municipal Hospitals in the interval of 1928 to 1949. Therapy was not stated. Eighty-seven per cent of the original group of 48 children were designated as "lymphoid" leukemia, but the exact composition of the 44 on whom survival data were available was not given. Fifty per cent of these patients were dead in three months.

Sullivan, Rice and Cassidy[30] summarized the clinical data on 65 cases of leukemia in children 12 years of age and less, seen at Children's Hospital, Washington, D.C., from 1938 to 1947. Therapy was variable, including blood when desired by the parents, roentgen rays in a few cases and varied therapy in others. Antibiotics had been used in some cases at some time. The available survival data on 59 of these patients have been analyzed. One-half of the patients were dead in about 2.5 months.

Bierman, Cohen, McClelland and Shimkin[31] reviewed the 103 successive cases of leukemia in children under 15 years of age admitted to the Pediatrics Service of the University of California Hospital during the interval of 1939 to 1948, inclusive. They gave detailed data on the survival of 76 children with "lymphogenous leukemia." They separated these into groups with (a) "no treatment," (b) irradiation, blood and antibiotics at some time of the disease, (c) "blood only" and (d) a group of 17 patients who received only blood, penicillin and/or sulfonamides. They found no statistically significant difference in the survival of the first three groups, but there was a prolonged survival of the group of patients (d) who received blood, penicillin and/or sulfonamides. It is of interest to note that the time required for 50% of the 59 cases (a, b, c) to die was 4.5 months and was 7.4 months for the group of 17 cases (d), treated predominantly with blood, penicillin and/or sulfonamides. The criteria for selection of this latter group were not given.

Southam, Craver, Dargeon and Burchenal[22] summarized the natural history of acute leukemia in 173 patients treated at New York Memorial Center from 1926 to 1948. Of the 150 cases on which survival data were given, only 53 were less than 15 years of age but, with the usual methods of analysis, no significant differences were found in the mean survival times of the various age groups. For these 150 patients it is interesting that the 50% survival time was 17 weeks and 95% at 40 weeks. Treatment was varied but did not include folic acid antagonists; it did include irradiation, urethane and nitrogen mustards, as well as blood, antibiotics and other supportive measures ". . . whenever indicated, regardless of the apparent hopelessness of a patient's condition." Analysis of the various methods of treatment used by the authors "indicates no notable therapeutic effect from these methods of treatment." Analysis of survival by cell type involved showed no significant differences.

Zuelzer[23] reported some preliminary notes on survival of children with leukemia that showed a log-normal distribution and survival times comparable to other articles reviewed (50% dead in 3 months, 90% dead in 9 months), but no details of the time period covered were given; hence, this series is not included in the analysis. He agrees with Southam et al. that those cases with leukopenia have a better prognosis for longer survival than do those with a leukocytosis.

Best, Limarzi and Poncher[8] give survival times for a group of acute leukemias of unstated age and sex composition, treated without antifolic acid compounds. They found 50% of 63 acute granulocytic leukemias dead in 3.4 months, and 50% of 43 acute stem cell leukemias dead in 3.7 months. Ninety per cent of these patients were dead in 8.0

and 9.2 months, respectively. Acute lymphocytic leukemias are not identified as such by the authors.

A number of investigators have given average survival times for groups of patients, without giving information from which the distribution of the survival times could be deduced. These include Booth and Rembolt,[32] 4.2 months; Falkenstein and Fowler,[18] 4.3 months; Craver,[19] 0.9 months and Simonson,[33] 4.0 months.

Discussion

Reference to table 2 will show that there has been a steady increase, from the 1920's, in the survival time of the child patient with leukemia. This might be attributed in part to the increased readiness to use and the availability of blood and antibiotics for the treatment of the complications of this disease. Increased awareness of the protean manifestations of the disease, particularly in its aleukemic form, may lead to earlier, more exact placement of the probable date of onset. The fragmentary data available on treatment for the leukemic process does not permit evaluation of the efficacy of the various technics utilized, but the clinical opinions of the various authors minimize its value. The exception to this is the work of Bierman et al.,[31] in which a statistically significant (5% level) increase in the mean logarithm of survival times of patients treated with blood transfusions, penicillin and/or sulfonamides is demonstrable over those not so treated. No confirmation of this finding was noted in the literature reviewed.

Rather wide variations in survival times of children with leukemia are noted in reports for the period 1930 to 1948; the reasons for these variations are not evident from the reports surveyed. The least favorable prognosis is that 50% of the children will be dead in 2.6 months, the most favorable in 7.4 months. The combined data* (chart 3) of the four groups of investigators[20, 29-31] publishing the most recent series would indicate that 50% of patients would be dead in 3.9 months, and 10% would be alive at 11 months. Results of a single case of long duration in this disease are thus meaningless unless interpreted in the light of the probabilities of its natural occurrence. The central two-thirds of this group of patients (chart 3) survived between 1.8 and 8.4 months after the onset of the first symptoms. These data are at least in part derived from a period in which antibiotics were not available and blood transfusions not as widely used as at present; hence, they certainly represent a conservative estimate of what can be expected from present-day therapy, excluding the beneficial effects of ACTH, cortisone or antifolic acid compounds.

Chi-square analysis[4] of chart 3 shows less than a 1% probability that the observed number of deaths at 0 to 1 month occurred by chance alone; hence, it can be concluded that other factors are operable. This deviation from expected values is presumed to be due to early deaths from intercurrent diseases, perhaps now preventable by the prompt and adequate use of antibiotics and blood transfusions. The remaining deviations from observations would be anticipated 41 times in 100 on the basis of chance alone. The entire distribution of observed values, including the aberrant values for the period of 0 to 1 month, when grouped in two month intervals, would occur, as shown, approximately 24% of the time on the basis of chance alone. These results confirm the decision that the log-normal distribution satisfactorily fits the combined data. To delete the "excess"

* The validity of this combination is open to some question on clinical grounds, since details of diagnostic criteria and treatment were not always supplied and may be dissimilar.

deaths occurring in the first month from our distribution would not significantly ($P = 0.05$) alter the time for the first 50% of the cases to die.

Summary and Conclusions

To establish a base line of prognosis for the "untreated" child with leukemia, the available literature on survival in leukemia has been reviewed. The applicable review articles (1927 to 1950), reporting a total of 428 cases of leukemia, have been analyzed.

It is demonstrated that the "average survival" of patients with leukemia is a misleading indication of both the most probable time of survival and the midpoint of the series.

The application of the simple, statistical technic of summarizing survival data on log-probability paper is demonstrated for the applicable series and is recommended for future reporting of similarly distributed survival data.

From these analyses, the physician can expect that 50% of the children with acute leukemia, given supportive therapy not including antibiotics, will die within a period of approximately 4 months after the onset of the first definitive symptoms. The remainder of his patients with leukemia will live considerably longer, about 10% for as long as 11 months. He can expect the middle two-thirds of his patients to survive from approximately 2 to 8 months. Thus, while there is no evidence of a definitive cure for leukemia, in many cases therapy should be planned to extend over a period of months, not merely days or weeks.

There are at this time insufficient data from which to evaluate the effects of cortisone, ACTH or antifolic acid compounds on the life expectancy of the patient with leukemia.

There is no evidence available to indicate that the prognosis in patients with granulocytic or monocytic leukemias of childhood differs from that of those with the more common lymphocytic leukemia. There is no evidence to prove that it is identical. More information is needed.

Acknowledgment

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SPANISH ABSTRACT

Pronóstico de supervivencia en las leucemias de los niños: Revisión de la literatura y proposición de un método sencillo para reportar los datos de sobrevida de estas enfermedades

Se hizo una revisión en la literatura de los enfermos leucémicos que no fueron tratados ni con antifólicos, A.C.T.H. o cortisona para establecer el tiempo promedio de sobrevida encontrándose que la distribución de este, midiéndolo desde el principio de los síntomas hasta la muerte del niño,

se presta a interpretaciones equivocadas de modo que el promedio de sobrevida como estimación pronóstica de dicho grupo de pacientes es desorientador.

Los datos completos de supervivencia de series de tales casos pueden resumirse en papel de probabilidad logarítmica y puede aplicarse esta técnica para hacer un análisis de todos los datos revisados. De dicho análisis puede esperarse que el 50% de los niños con leucemia exclusivamente tratados con terapeútica de sostenimiento (sin antifólicos, A.C.T.H. cortisona o los mas modernos antibióticos de cuyos datos se carece) vivirán aproximadamente 4 meses después del principio de los primeros síntomas definitivos. Solo cerca del 10% de estos enfermos sobreviviran hasta 11 meses. En consecuencia, debe planearse una terapeútica que se prolongue por un periódo de meses y no únicamente de días o semanas.

En el momento de esta revisión no pudo hacerse una evaluación crítica de los efectos del A.C.T.H. cortisona o antifólicos sobre el tiempo de supervivencia de estos enfermos ni tampoco pudo demostrarse que el pronóstico de supervivencia de niños con leucemia linfocítica difiera del de los niños con leucemias menos frecuentes como las granulocíticas o monocíticas.

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Round Table Discussion

PREVENTIVE PSYCHIATRY

HENRY H. WORK, M.D., *Chairman,* Louisville
MAURICE J. LONSWAY, M.D., Clayton, Mo., and ALVAH L. NEWCOMB, M.D., Winnetka, Ill., *Secretaries*

Chairman Henry H. Work: The kind of problems that one sees and one thinks one can do something about as far as we are concerned in pediatrics must, I think, be related pretty much to the early years of life. I would like to give you something that I have recently discovered: a nice formation in addition to our own mental concept of what is happening to the personality. I don't know if it fits your experience but I have found a great deal of good in it.

In the preparatory work last year for the White House Conference, Dr. Eric Erickson was called on and provided some very excellent material which he is presenting now in book form, in a book called *Childhood and Society,* and also in a publication of the Macy Foundation called "Symposium on the Healthy Personality." He breaks down the changes in personality relating to growth in the following way: the first year of life, we all think of and know as a period of taking things in. The child lies there and his responses, by and large, are in terms of what goes into him. He does this right from the day he is born. We know that he doesn't have the 5 senses very well organized, although he possesses all of them and we know that his motor responses are diffuse but they get more and more orderly during that year. In terms of what he wants from the outside world, Dr. Erickson feels that trust in his environment is his major concern. We may call it dependence, a need of warmth, etc., but I find the word trust very acceptable as a basic word for the child's reaction to the environment during the first year. Much of our adult mistrust and trust goes back to a very early stage. Not only the first year but in the very early relationships of mother and child. Then he stands up on his feet at the end of that year and he starts to move around and during the second year of life he really undergoes more changes than he will ever undergo again. His growth pattern doesn't change quite as much, but between that first and second birthday he changes tremendously in terms of knowledge and learning. He learns to feed himself, to talk, to control his eliminations, so that he goes from a stage of dependence to almost independence. Dr. Erickson calls that period the development of autonomy. When this is not obtained, he feels that the result is primarily a development of shame. This arises chiefly in relationship to those normal activities which are commonly called "dirty." In the next 3 years, the child's locomotive skills increase, and he begins to show interest in his own activities and in his own body. Here again a conflict arises with parental standards out of which comes, according to Dr. Erickson, either initiative or guilt. The school age years offer the

From the Annual Meeting of the American Academy of Pediatrics, Toronto, Oct. 22 and 23, 1951.

opportunity to try out this initiative in an effort to apply it to the task. Here, also, the child meets the group and learns something of his role. The resultant feelings engendered in this period are those of industry, or when difficulty arises inferiority. The latter is complicated by the child's difficulty in establishing his own sense of values particularly if the group standards are in contrast with those in the home. Somewhat beyond the pediatric range are those levels established in puberty and young adult life; the former producing either identity or role diffusion, the latter either intimacy or isolation. In the application of such knowledge, we feel that the pediatrician working through and supporting the mother has an opportunity to point out this knowledge, to help her give the best warmth she can, and, in understanding the child, help her to tolerate him enough to allow him to learn for himself.

Question: Do you feel that toilet training has its place in the psychiatric problems of children?

Chairman Work: I would like to hear what someone else thinks about that.

New Speaker: I would like to say that I tell my mothers that the child should go into the second year and see that everybody else uses the bathroom for that purpose and the child usually develops a willingness to do the same thing. But my problem was illustrated last week when a mother came into my office and was following that advice and apparently there was some friction between her son and herself because the child, 2½ years old, was deliberately soiling his pants and enjoyed both the being soiled and the consternation he caused his mother.

She came into my office very upset, trying to shame the child. In spite of my efforts to calm her down and stop her from talking like this in front of the child, which I thought was damaging, she continued. She blamed me because I had told her not to be rigid in toilet training.

Chairman Work: One learns to be extremely wary of a certain group of patients; they want very exact instructions about how to do anything. I find them difficult to deal with because I know that if anything goes wrong they will be back next week and say "I did exactly what you told me to."

With the mother you are speaking about I wonder what the trouble is because I am sure that your approach is quite valid and quite accurate. Does it mean in this particular situation something happened over which you had no control?

First Speaker: I am sure there is some friction between this mother and her child but what I am trying to prevent is the mother's going ahead and doing further damage. She wants real action now, but I think she has already done enough damage.

New Speaker: In prenatal care little is said to the mother about this preventive pediatric psychiatry. I think that we are beginning to realize this. We stress albumin studies, blood pressures, etc., and neglect preventive pediatric psychiatry.

Another thing in this pediatric advice is that we have to be constant, patient and calm. Sometimes when we introduce ideas to these mothers I am inclined to suggest a period of 2 weeks before we expect any changes. You won't get a change in a situation much before that.

Chairman Work: So that you feel that in terms of this particular situation there still is room for an experimental period.

New Speaker: Dr. Work, I agree with many of the things you have said but I came into this meeting looking at this problem from a different point of view. For instance one of my concerns is the mother herself, who is a dependent individual, transmitting her own anxieties and dependencies to her children, and I am concerned with what to do about that kind of mother to prevent the occurrence in the children.

Chairman Work: I think we must proceed with our work on the thought there are some things that we cannot do. For us to attempt to do the whole job is attempting to take on too much. We see in our ordinary contact with people some mothers who do an extremely good job and don't need any particular help and we see another group who are really so difficult that you can't cope with them. For example, the one I quoted is a really schizophrenic mother. She has a child and society will be responsible for that child but we are not going to cure her in the process. I think that what you are doing probably does more good than you think it does. For example, the woman whom you realize is dependent—the fact that she does depend on you enables you to do something for her. She will accept your reassurances so you can get something from the association. You can set a pattern in the early contacts with her so that she begins to see that what you say does make sense. I think that when you start out with a mother you are not going to do a lot for her the first time unless she has been preconditioned to you by some other good doctor. But over a period of time she may accept what you say and it may be that it will get a lot easier.

I think we might discuss the point of just where out job ends. It is an extremely important one. It raises the difficult question in the handling of the situation—when you are trying to eliminate a symptom such as temper tantrums whether you should eliminate it in favor of another symptom which might be causing more difficulty. As pediatricians we have always given advice to parents from time to time to ignore something. Rather, it seems to me, our pediatric job is to help parents accept that kind of behavior. There must be a meaning for that kind of behavior; children don't have temper tantrums merely to attract attention.

The pediatrician should, when it is apparent that the mother is a rigid individual, try to help her accept the things that her child does. It isn't very easy for her to do this but she will do so with your help. It isn't just loving him but being able to accept the things which seem so wrong to her.

New Speaker: I just want to say one thing in this respect: I don't try to make every patient conform with what I believe in toilet training or even in breast feeding. I run into patients to whom I feel breast feeding would be very disadvantageous. They are not ready to accept it and the child would become more upset instead of more secure.

Chairman Work: We have been swamped with much revolutionary material in child care and I don't think that we have thought enough about medical indications and contra-indications for some of the procedures. We should exercise clinical judgment using a certain known group of observations about what happens to children as they grow and then try to apply that in specific situations when the mother is either a disturbed individual or potentially so.

New Speaker: We talk about certain types of mothers but what about there being certain types of children? Can we tell a mother that her child is a certain type of child and should be treated thus and so? I am thinking in particular of the hyperactive child: the mother is unable to control the child and he goes on his way. If that child could be handled properly when young, he would be a very exceptional citizen. But if mishandled, he will become antisocial.

Speaker: I would like to recite a philosophy of my own since we as physicians believe that we have a role in the emotional field. Then I feel it is logical to believe that we have a broad view, in terms of preventive psychiatry, radio, newspaper, handing out leaflets, booklets, preparing parents for what is to come and encouraging them to read the right book, listen to the right people, from a broad educational point of view. We also have the narrow problem concerned with Johnnie Jones in our own office—this one single appointment that is coming in now. We then find the necessity to explore the meaning of the symptom. One of my favorite questions to students or candidates before the Board is to say, if you have your preference, would you rather treat a temper tantrum or night terrors. They fall right in, they would much rather treat a temper tantrum.

When we have a child in our office whom we mentally catalogue at a glance as an emotional problem we encourage the mothers or we refer the mothers to reading material or expert opinion. I wonder if we shouldn't try, and this is the point of philosophy, to agree that we should classify patients in one of three groups. Ones that we know from our own experience and own lives as children who have normal reactions to abnormal situations. They came out of it all right. All of us came to wherever we are through conflicts. We reassure, are sympathetic, and listen. Now in the second instance we are not sure of the meaning of the symptom, not as doctors, but just as persons. We are not sure of the meaning not as psychiatrists, pediatricians, but as adults working with children and trying to see the situation from the point of view of the child. We are not sure of the meaning of the symptom.

Then we pick up the telephone or pull out the text book and work this through curbstoning, helping one another.

Then we have the third situation: we have no more business in this situation any more than I have any business in the middle of a peptic ulcer. Our business as pediatricians in this third case is to recognize that this is strictly a major psychiatric disorder of the mother or the child or both. We should do our blood counts and examinations and get that child out from under the extra attention of the medical situation and put that child where it belongs just as strictly as when it belongs in the hands of the surgeon. We have tried in our undergraduate program to impress on students at the junior class level the importance of being able to distinguish between these groups, that they can work as humans, not as doctors necessarily, but as scout leaders, advisors, etc., being sympathetic, and listening—rather than to work through the text books.

Chairman Work: You raise this question of the limitation. Where do we stop? Do we have any

signposts? We have been talking, for example, about anticipatory guidance and how we can give to a parent some things that can make it easier for her to anticipate a thing when it arises. We have to anticipate also—any of us who have seen a lot of mothers can guess what problems her child is going to get. You can spot the efficient young business woman who knows how to run an office like a clock, but who suddenly finds herself first in marriage and then pregnancy. With such a background we can often anticipate a colicky baby. How then can we use our anticipation, our knowledge of the clinical syndrome, to tell us which patients are going to get into trouble and which patients we are going to have to send on? I think one clue we can find is when the difficulty between mother and child gets so severe that she loses her perspective in even talking about him. If she gets to this point it is totally frustrating to her; she will be resigned and has given up, feeling that there is no hope and this is just the end.

Certain other clues are important: when the symptom has either persisted for a long period of time or has grown progressive. That, I think, on a quantitative basis makes one say more help is needed. For example, we are faced with enuresis all of the time; it is a common thing that we deal with but I think we can be assured that in the treatment of one you have more luck with a 4 or 5 year old than a 10 year old in terms of time.

As we deal with stuttering we realize that it is more serious in the older child because it means greater disturbance at that time.

New Speaker: I think if you had a bad situation that you find impossible to manipulate you might just as well quit trying. If you know there is domestic discord you can explain to the parents what it is doing to the child but if the discord continues I am afraid you are not going to get very far. We see that the manipulations of situations is as important as psychiatric care. I care for an orphanage where most of the children come from broken homes and we have on our staff some of the finest psychiatrists in the city, including analysts, and these children come with all sorts of problems and they improve a great deal. They don't get well, but they do improve and I think it is as much the fact that they have been removed from their home environment into a warmer and loving environment as it is to the psychiatric treatment and the analysis that they receive.

Chairman Work: When mothers come to me I outline the fact that I consider my role to be that of a consultant and advisor, not as a person who is primarily responsible for the child's welfare. I emphasize that they have to accept the responsibility for his welfare, his total welfare; that I am the person to whom they can come for advice but that the final decisions are up to them. This is the best preventive psychiatry.

You can't force patients to go for psychiatric treatment. I have a case here where the mother was extremely frustrated witih a rivalry situation. We tried to help this mother in the situation. We didn't get the situation soon enough but noticed that the mother gave all her attention to the baby who was our patient. We realized that the situation was growing intolerable between herself and the older child because she could not accept the jealous behavior of the older child toward the baby. Because she did not accept it it grew worse. We thought that perhaps this went beyond pediatrics and belonged in psychiatry; how could we get this mother to it? Well, we did not use that word initially, but we would allow her to describe the situation and tried to comfort her and to get her to accept the difficulties under which she found herself. When she got to the point of saying, "I need help," we began to point out that there were certain places where she might get help. Later she came to us saying, "I am at the end of my rope. I would like to get help for my child." Then we were able to refer her and to make the referral stick.

New Speaker: How far would you let a child go with natural curiosity? Turning on the stove, electric outlet, etc., those are the things that the mother asks you constantly and we as practicing pediatricians should know.

New Speaker: Don't you think we tend to make too much of these problems?

First Speaker: Have you ever stopped to think how many men are in the penitentiary or insane asylums, or the number of neuropsychiatic cases we had in the army from things that started in early childhood!

Chairman Work: When it comes to discipline there is no specific answer. Each instance requires particular and individual advice and depends on what the mother's past has been. If you are trying to do preventive psychiatry you would hope that you have known her as long as she has had this particular child. Now that, unfortunately, does not happen too often.

New Speaker: How soon do you tell a child that it will have a brother or sister?

Chairman Work: I think you start at the fifth month of a pregnancy with a child who is 13 months old and start talking about a new baby. He learns words and pretty soon picks up words including "baby."

Chairman Work: I was very impressed with Dr. Klein's talk yesterday when he talked about the need of the practitioner as he saw it. He made the statement that one of the things the practitioner wanted to know was how to translate the art of medicine into the scientific care of the child. It was a very interesting statement because it seemed to me it could be put into the opposite way and be equally meaningful—how to translate the scientific care of the child into the art of practice. I am sure that what Dr. Klein does in his everyday work is to take the scientific material which he gets from his observations and turn it back into the art.

If there is anything that epitomizes what one can do in preventing disorders of behavior, I think that is it. Taking the knowledge of how people behave and turning that into the art of our practice, thereby helping the mother and the child and theoretically the whole population. It has always been our effort in pediatrics to work with young children and I think for as long as there has been pediatrics we have been trying to not only keep children well but to help their general social well being and emotional well being. The root of what is termed prevention lies in our own practice. Considerable knowledge in the field of psychiatry has been handed down to us; this material came to us because we do deal with the small child and the psychiatrists have been concerned because they don't deal with little children.

They point further and further back in the order of life to periods that have always been of our concern. The psychiatrist points out to us, too, very clearly the relationship between the mother and the child. Now I know all of us wonder how to approach the mother and what are the routes we use in dosing the child through the mother. Our concern is with her because we want her to help us with the child. Sir James Spence says that, from his point of view, the role of the pediatrician is support of the mother. That is one of his major functions. I think we can see from our own case material that there is a great deal of truth in that and the preventive role seems to lie in that phase.

I would like to give you a couple of cases that will exemplify this dual problem. The problem of using our knowledge which we have formulated in our own practice and observations and the relationship of that to the mother, what she is and what she has become since she was a child. The importance of these cases, it seems to me, is that they show not only that the child changed from a flat to an upright being in the second year and gained in proportionate height and weight but that when he does that it changes the family situation. She has to act differently toward him than before. We have seen for a year a mother who came to us when the baby was 4 weeks old, a very healthy, good sized baby, one I think anyone would be proud to have as a child. This mother was about 40 years old, which was no particular handicap in itself except that she had already had 2 families, so to speak, 3 children 20, 21, and 22, then 2 children, 13 and 14, and then this baby. We didn't see her during her pregnancy, but when she came to us she was in distress. The baby was big and healthy and activity was the thing that she most complained about. Now one of the things she did poorly, and you have all seen this in your office, was the way she held the baby. It is so easy normally to cuddle a baby that we forget about the difficulties sometimes. I used the word rejection too much yesterday so I won't use it today. Let us say that they are not fond of it at the moment.

I illustrate this as an example and perhaps some of you will tell us of the cases you handle.

What does one do with the mother who is really mentally ill but who may have a child. "Any woman can have a child but to be a mother is something else," as Siwe has said. We see women like that who are a real problem to us. Trying to prevent difficulties in their children offers greater challenge, one that is hard for us to meet as pediatricians but the thing is they come to us as a pediatrician because they have a baby and they feel they should take the child to a baby doctor. In trying to think how we work on this problem, I think it is worth while to talk about some concepts in the psychiatric field which are of importance in the stages of development as we use them in our pediatric thinking.

It sometimes seems that when we reassure a patient we are doing no very definite therapeutic act. However, we accomplish something merely in the process of reassurance.

The very simple things that are needed can be pointed out; the warmth which a mother can give,

the manner in which mothers can take on and get used to the rhythm of the child, and also the opportunities a mother can, through our help, give a child to try himself out.

New Speaker: The point that you have brought out is that the mother is very valuable and then there falls back on us the further problem of how we can help the mother to become trustworthy, which revolves around her ability to trust herself. I think one of our great difficulties as pediatricians is that we frequently don't trust the mother. We have good reason not to trust her, but how can we so relate ourselves to the mother that we will help her to build herself into a person the child can trust? One of the things that brings us to is our own feelings which are so significant in this. Frequently we don't trust the mother because we are going to feel so disturbed ourselves if the mother fails us in carrying out some of the programs that we have entrusted to her. So the status of the physician in his relations to the mother and to himself enter the picture. So when we talk about the need of the child to trust we have got to establish a relationship between the mother and himself in which he can do this. Many times the mother has never had any dealing with anyone in her life who treats her like an adult. We have to be extremely careful that we don't continue in the pattern and become somebody she turns to as she turns to her mother, father, etc., and who finds in the doctor someone who relieves the necessity of trusting herself.

New Speaker: Many of us have had our experience in hospitals and many in training in wards, where the whole attitude is to get rid of the mother. Where the attitude, certainly of the nursing staff, of the house staff and many times of the physician, is to get rid of the mother as fast as possible. I think that is an interesting point to remember when we are trying to deal with these mothers.

New Speaker: I am beginning to realize that we have an obligation to believe in our own observations and finally come to the conclusions that some of the things that our teachers taught us were wrong. To get to that point is sometimes quite a step in our own emotional evolution.

New Speaker: Dr. Work, I am confused in the matter of discipline of children and I have a little trouble in answering the questions the mothers put to me in how to discipline a baby and how much a small child can have. I am having a little trouble in formulating my own ideas about whether a little 3 or 4 year old should be allowed to run around like a wild Indian or not. One of the first times it crops up is in children who are over 4 or 5 months of age, well over the colic stage. I find quite a few mothers who have babies who cry for no reason that they can figure out. They want to know whether the baby should be allowed to cry itself asleep or whether they should rock the baby. Also, how much of this activity do you have to put up with in young children and how much discipline can you give a child without injuring his personality?

Chairman Work: The whole problem of discipline has changed considerably in the last 30 years. Unfortunately, this means that young mothers have grown up in a rigid demanding framework, and they are confused by suggestions that they be lenient with their children. This they often do not know how to do. As we have discussed with other problems this morning, one can say very briefly that it is our job to help them set limits to the behavior of their children. We can go on to discuss this in terms of sleep difficulties.

We previously would treat a child and a mother as the classic structure in child psychiatry but now we begin to see that we have to bring the father into the session and very frequently have joint conferences between father and mother to iron out difficulties in handling the child. I wouldn't be a bit surprised but many of your situations result from friction between mother and father.

The problem of sleep resistance is rather new and it is certainly one of the outstanding problems we have to deal with.

New Speaker: It has always been my plan to limit the amount of sleep during the day and I find that it helps a whole lot.

Chairman Work: How do you limit the amount of sleep during the day?

Previous Speaker: The mother gets the baby up after an hour and a half, say when it is 4 months old.

New Speaker: The majority of babies I see are good babies until they are about 8 or 10 months, then they begin waking up. The mothers bring them in saying they are up every half hour during the night.

Chairman Work: I will tell you my approach to this and you can do what you want with it. In terms of observation I think there is one thing about child sleep and that is that the child who has not had enough sleep is a worse sleeper than the child who has had an adequate amount of sleep.

I strongly suspect that there is a good etiologic basis for that. In that point I would disagree with you. I remember that when mothers would complain that the child would not go to bed at night I would tell her not to give him a nap in the afternoon. I now think the opposite is true—if a child has a good nap in the afternoon he is more apt to go to sleep at night than the child who misses his nap.

You have certainly described what are relatively common phenomena. Most small babies sleep pretty well, a normal baby settles down quickly to a.m. and p.m. naps and I think that fits pretty well the constitution of the household. Now Gesell points out that the baby from 4 weeks to 4 months tends to be more awake at night than he is in the early morning. He suggests, but I think it is a very difficult suggestion to carry out, that our daytime activities with the small baby be focused in the early evening and goes so far as to say "bathe the baby then." Family situations for the most part do not allow time to follow this suggestion, but I do think that it is a situation we ought to take advantage of in preventing the difficulty that you are describing at the 8 month period. That is a classic period, a period where difficulties begin.

By talking to the mothers about taking advantage of this wakefulness at this early infancy and making the child more a member of the family group, sometimes the baby is made much more comfortable and goes off to sleep at 8 or 9 o'clock. Somewhere around 4 or 5 months he shows that he is not quite up to that because he is not sleeping as much in the daytime and will go to bed earlier so that you put him to bed earlier when he is sleepy and it gets closer to that 6 o'clock period.

I wish we knew what the problem was behind the 8 month thing. I think we know more about the situation described as occurring after a year than we do about the 8 month situation. We can, however, predict in a lot of babies and particularly if a mother is a tense individual, maybe like the intellectual faculty people you mentioned, that she is going to have the baby who may get into difficulty at that time and she is liable to be more concerned about it than other mothers might be.

An interesting thing is that when there are 10 children living in one room you don't have sleep problems to any great extent. They may even fight for a place to lie down on the bed. I am sure that this 8 month difficulty relates to crowding, to insecurity of the mother, and maybe the fact that she is a little more free. As she is able to go out a little more she is anxious about going out. Certainly starting with the mothers you anticipate will get into that difficulty, at about 6 months you begin by telling them that the difficulty might arise.

Dr. Spock has pointed out that it can be a fairly serious situation; when you get the very sleepless 8 month old and he gets to the point where he doesn't sleep until 1 or 3 o'clock in the morning, then you really have a family difficulty. I think it is hard for the pediatrician to handle but it has been Dr. Spock's experience (and I have seen it in a fewer number of cases) that getting the mother in and the father in, one can get them to be more easy about the situation. When I say that we get in to the matter of therapy—what do you do with people? What makes them change? Well, for one thing, many parents have gotten around the early part of the difficulty and they have come around to this thing about sleep. They don't want to be bothered with the baby at that point so the therapy is to get them to calm down and accept the child's behavior as a natural phenomena, because it is natural for babies to be relatively wakeful at that period. We allow them to blow off their steam about the baby and say how much the baby is interfering with their activities and then ultimately get them to a common approach to the situation. That is one of the things we are learning in child psychiatry, for example; that where we would previously treat a child and mother, now we have joint conferences between father, mother and child.

New Speaker: Do you use drugs at all?

Chairman Work: Not in the preventive aspect of it and not in the milder cases but certainly in the child who is keeping people up until 1 o'clock in the morning.

After that period, somewhere around a year, you don't have many complaints about sleep; then you get into the 14 month group who start an entirely different sleep problem. I think the first one is intrinsic in the child just not being ready to go to sleep.

Now the toddler is quite a different situation—he doesn't go to bed quite as early but probably plays around after supper. He may have an older brother who doesn't go to sleep at this time or an older child in the family. But his difficulty is attributed mostly to coming into a relationship with his family who know him, want him and understand him and he is beginning to get a fear about leaving. It is in many ways one of the psychopathologic situations which is fairly normal to all children; all children go through this. They become aware of the family, how good the family is, and

begin to have minor fears of various kinds because they are beginning to perceive things to have fears about and then they relate that to leaving the family. In those children I think the same type of parent we have discussed gets into the same difficulty although the cause as far as the child is concerned might be quite different. It really then is a fear situation, wherein the child lumps together his fear of the dark, noises, etc. That problem becomes a problem when the parents get into a quarrel with each other about this.

Chairman Work: You don't have to keep the child downstairs for a half hour to quiet his fear; you just bring him down and give him assurance and put him back. These things get bigger and bigger as you say and they get bigger and bigger because the parents get more and more inconsistent about what they do and the parents get afraid. We have to reassure them, take away the fear that it is not going to hurt that child to let him cry and it will not kill him or ruin him for life if they have to put him in bed and let him bawl it out a few times. If the child cries for hours every night then you know there is something grossly pathologic there.

New Speaker: How do you feel about the baby sitter and how soon the baby sitter should enter in. My experience with my own little 3 year old who for about 6 months raised Cain in going to sleep was that when we get a sitter in, she goes to bed and sleeps the whole night. So maybe there is some good in getting them used to other people.

Chairman Work: The child around the age of a year and perhaps somewhat before is quite distrustful of strangers. I think one of the most disheartening things is to take a year old child to see his grandparents for the first time and he doesn't like them and pretty soon they don't like him.

The problem then of strange people seems to me is—how strange is the person? If you start having a baby sitter at a very early young age, she is no stranger. She becomes a member of the family. It gives the parent a chance to relax too. I am particularly interested in trying to think of situations where we do have to manipulate; we can't do gross psychotherapy on everybody.

We have as a matter of fact added the sitter to what we think is preventive work-counselling very early. We do this with the mother who comes in at 4 weeks or 10 weeks and just as a routine question we say, "Are you going out at all?" Many mothers haven't left their baby at all and in doing so they are building up something that will be hard to break down. They are getting away from their husbands, they are not being a married couple. I think we as pediatricians are the only people who see that situation and we sometimes have to remind people that they are married. They forget that they have a husband because a baby has come into the situation.

New Speaker: Will you tell us something about nightmares?

Chairman Work: Nightmares occur in children who have other fears and a lot of anxieties they are working out in their dreams. If they become a chronic, constant phenomena, you will find that the child has other things that are bothering him in the daytime as well. You are not treating nightmares as such, you are treating a fearful child. Every child probably has a few nightmares or has temper tantrums. If they are just beginning, the mother has to accept it as a relatively normal situation and give the child a lot of reassurance. I have a pamphlet here called *Some Special Problems of Children,* published about 3 or 4 years ago and it is of great help. It is now published by the National Mental Health Foundation, 1520 Ray Street, Philadelphia. You may give it to parents on these special problems.

Round Table Discussion

PREVENTIVE PSYCHIATRY

SHERMAN LITTLE, M.D., Buffalo, N.Y., *Chairman*
ALVAH L. NEWCOMB, M.D., Winnetka, Ill., and KENNETH T. KNODE, M.D., South Bend, Ind., *Secretaries*

Chairman Little: This session has a title of "Preventive Psychiatry." I am not sure that it is an entirely correct or happy one. Psychiatry is still a bad word to a good many people, including some physicians, yet it has a real connection with the kind of thing in which we are all interested. What we will discuss is psychiatry in the sense that we are concerned in understanding and helping people, in this case, children. Yet it is not psychiatry in the sense that we are concerned with long term treatment of severe disturbances of adjustment. It is an application of psychiatric knowledge and skill by pediatricians within the framework of pediatric practice. The emphasis is on preventing disturbances in adjustment or on correcting early and relatively shallow-rooted ones.

For a long time many pediatricians have been giving a great deal more than good medical care to sick and well children. On their rounds and in their offices they have consciously and unconsciously helped many children through helping their parents. They help parents by supporting, encouraging and advising them in the difficult job of being parents, and in so doing, they indirectly but concretely help many children. It isn't easy to do this, at least I don't find it so. In the first place, we aren't trained for it. If we develop any skill at it, it comes from experience, which can be painful and slow, and from something that we call intuition. As a matter of fact, our medical training, at least that part of it concerned with our handling of the patient with a medical problem, is often a serious drawback. We are accustomed to telling people what to do. We say, "Take these pills every 4 hours; drink lots of water; stay in bed until I tell you to get out." The patient is relieved and happy. This is what he wants. We are trained to do this, and up to a point it is what we should do. We have been called in to tell people how to cope with something from outside themselves (outside themselves psychologically if not actually physically) which is attacking their physical body. Most of the time the patient feels no responsibility, no guilt in being ill. He doesn't feel defeated and inferior because he's caught a cold or has the flu. Of course if he has lues, he usually doesn't boast about it. The point I am trying to make is that he doesn't resent being told by the doctor what to do to make himself better. It is not a part of himself that is at fault, it is some external agent which is attacking him.

However, it is quite different when you are dealing with an individual with a problem of adjustment, or a parent of a child with behavior difficulties. They feel that this is something which concerns them, something for which they are responsible, something which indicates that they are at fault and in some way are failures in the job of being parents. It is not easy for people to change their thinking and behavior around things which do not touch them too closely and it is even more difficult when it is something which to them seriously questions their capabilities as parents.

Difficult as this is, this is not the major difficulty. The major difficulty is that out of their own past experience, particularly in childhood, they have acquired many concepts and attitudes, some of which are applicable and useful as parents and others which are inapplicable and perhaps basically unsound. It is these concepts and attitudes which largely guide and determine their behavior as parents. All of us do this to some extent even in the face of evidence which to others makes it obvious that what is being done isn't working.

In spite of education, advice and suggestions of others, parents are apt to persist in methods which will not work in their particular case and might not work in any. If you go into a situation of this kind and attempt to handle it authoritatively as you would a case of tonsillitis or pyelitis, you find yourself met with a considerably different reaction. Although the parent says he wants advice and help and you offer what seems to you to be very sound stuff, it either does not seem

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From the Annual Meeting of the American Academy of Pediatrics, Oct. 22 and 23, 1951.

to work in spite of earnest endeavor on the parents' part or to your surprise you find that they are not carrying out suggestions that you have made. This is at times apt to be annoying, and one's impulse frequently is to step in in an even more authoritative fashion. If, however, you stop for a moment to think what is going on, it may become clear why good advice is not working. There are several reasons why it may not be but the most important one is that basically you are suggesting to the parents that they modify a pattern of behavior which has been built up from early childhood. In other words you are asking the leopard to change his spots overnight. Furthermore, you are implicitly suggesting that his basis of operation as a parent is false and incorrect and that he give up what has seemed right and familiar to him and try to use something which is both unfamiliar and may from certain past experiences actually seem wrong to him, or at least very threatening. Of course there always is some possibility that what seems like good advice to you may actually not fit this particular parent and child because, as you know, behavior is not stereotyped. It is still true that there are a number of ways to skin a cat.

I have perhaps made enough of this point that one needs to use a different approach in dealing with problems of behavior than one does with a strictly medical problem. One needs to give up the authoritarian approach because it is inapplicable to this kind of situation. What then can one do that will be effective?

Various people, of course, have through experience worked out ways which are reasonably effective for them. Important and effective as this can be, it is even more important in the long run to define and understand clearly what one does and why it works or doesn't work. Only in this way can understanding and skills be improved and, to some extent, transmitted from one physician to another.

What is the kind of knowledge and skill which can be most effectively used by a practitioner of pediatrics? To my mind it is something that comes basically from psychiatry but has to be modified or changed to fit the setting of pediatric practice. I think it is useful for a moment to look at what another profession has done in a related area. I would like to speak for a moment about social workers because the field of social work has adapted psychiatric understanding and psychiatric skills to the professional job of social work.

I use social work as an example because I believe there are certain areas of professional practice in social work and in medicine which are very similar and at times even overlapping. This is in the area of helping with external problems which confront parents. The social worker may be dealing largely with problems of social nature, while the doctor helps the parent with the reality of being a parent dealing with children's reactions or the feelings which are stirred up by illness and operations. The area of responsibility is different but largely so in terms of knowledge and special conditions, not in basic skill.

To some, my use of the social worker as an example may seem inappropriate. There is still a hangover of associating social work with giving relief or with some of the negative reaction with which psychiatry has to deal. Unless you have had the good fortune of working closely with skillful social workers, you may not be aware of their professional and understanding competence in helping people with difficulties. By and large they confine themselves to helping with problems in the reality situation, in the situation or environment of the individual. Many people helped also have internalized problems of greater or less degree, but it is often gratifying and at times amazing how the individual is able to cope with his internalized problem as he is given understanding help with those problems which press upon him from without.

The social worker's most useful tool is the ability to conduct a skillful interview. The physician needs the same tool. Through this means parents can help to sort out and clarify the most pressing problem and to decide what are the possible contributing causes. Having been helped to achieve some order out of what has seemed to be baffling chaos, the possible approaches to the contributing causes are examined and the parent is encouraged to decide on a course of action. Through all this, the various conflicting feelings of the parent are calmly accepted as they are brought to light even though some of them may be a little surprising. It is this which gives the parent a feeling of acceptance and which often frees and encourages them to go ahead in some positive direction.

When the practicing physician has the necessary understanding of human nature and the skill in interview to do this with parents, a tremendous amount of emotional disturbance can be prevented. As a matter of fact, many seemingly serious situations would be helped without recourse to child psychiatrists or child guidance clinics. It is important to be clear when one has gone as far as one can and when to refer to specialists in child psychiatry. Perhaps this sounds as though

I were telling you to be psychiatrists and perhaps you think that to do this would take much time. I know from my own experience that what I have suggested can often be accomplished in 2 to 3 interviews. These do not need to be an hour long. Perhaps one at the beginning of a half to three quarters of an hour, and after that it can be done piecemeal following an initial clarification. A few minutes at the end of an office visit or a house call will often do the trick. Some of it can be done during your phone hour in the morning.

This will not prevent or solve all problems. If it would, psychiatry and child guidance clinics would have no function. There will probably always be a significant number of parents and children with severe internalized problems who will need the special skills of the trained child guidance clinic team. You can help to get these people to the help they need.

One other thought comes to me, and that is that you may be skeptical of the effect of this or the methods I've described. I can only say that it helps parents to help themselves.

There is nothing that licks frustration, discouragement and the unhealthful behavior which often accompanies these feelings like beginning to do something effective about a problem. If parents can get from their contact with the doctor a feeling of his acceptance and understanding of them as people, some skillful help in critically examining the possible causes for the difficulty and some support for their own plan of solution, they are often enabled in time to work through the difficulties in quite a satisfactory fashion. As a matter of fact, there is no sound solution of problems except in this way. No one can solve others' problem for them, nor ever tell them much what to do, but you can help people to use their own knowledge and judgment. Neither the doctor nor the parent should be distressed that they do not completely understand all the cause of the problem. Understanding or insight, as it is commonly called, is a fairly feeble problem-solving tool. Much more important is the feeling of acceptance by others which gives us courage to try, some slight help in clarification, and the satisfaction in our own achievement which keeps us going. These are the kind of things which the doctor can give to parents.

Now as to evaluating the child himself. It is not always easy for us to do this because we get very little training in our formal pediatric training in being able to skillfully evaluate children. However, if you start with the observable behavior of a child and not just one small observation, you can get a good many clues as to what is going on. Children handle their feelings in different stages of development. You can observe this and combine this with your own knowledge of the parents and the history which they give and you can often be pretty accurate as to the amount of disturbance which is present.

One of the best of the observations which can be made is to notice how the child handles his feelings and to relate this to some rough standard in your own mind of the way a healthy and happy child of that age would handle feeling. Then you want to find out if his reactions are typical of his general reactions or if they merely represent a reaction to some fairly immediate experience. If what you see seems to be a fair sample of his behavior in general then it is significant.

For example, as you see his reactions to situations and thoughts which produce feeling you can note if he responds appropriately. Is he too cheerful under circumstances which would naturally bring out discouragement or anger? Does he dare to be friendly? Can he show appropriate disappointment? Naturally your own bias colors your observations, particularly if you feel that small children, especially boys, should always be brave little men and not cry when they skin their knees or should die fighting rather than temporarily accept defeat.

However, if you observe carefully and subject your judgments to critical examination, you ought to be reasonably correct. This helps because any child who does not on the whole handle his feelings appropriately is bound to have trouble. It may be obvious trouble or it may be trouble only in the sense that it is a sign of an inadequate and limited use of his total self. After all, we want children to be able to use all their abilities, physical, intellectual and emotional. Too many people are only partially functioning because some of their emotional life is not functioning in a full but controlled fashion.

Now a word about the specific way in which a pediatrician can be of help to a young mother—to make the situation clearer—a mother with her first baby. I want to emphasize this for 2 reasons. The first is that this first experience in being a mother and this first beginning relationship with her baby are very important times. The second reason is that for the past 40 years there has been accumulating pressure on mothers to make them feel less capable as mothers. First with the advent of scientific feeding the implication to mothers was that feeding was a science only for doctors and nutritionists to understand, not a mere mother.

Secondly, with the advent of modern psychology and psychiatry, we implicitly say to mothers, "Don't trust your natural, maternal impulses; beware of your own thinking about bringing up your children; child rearing is a science, needing great knowledge and fraught with many dangers. One must be a scientist to bring up children and obviously you are not that."

All of this has knocked the props out from under mother's confidence in themselves. It is perhaps an inevitable and painful stage in our development of genuine knowledge but it is mighty hard on mothers in the process. Gradually, as you are aware, we are recognizing that much of what mothers have done out of the living experience of the race is in many instances sound and "scientific." But we come to this slowly, we are skeptical and have to be convinced and meantime mothers are being put through the hoops.

From this, at least to me, it seems clear that young mothers need a lot of support and encouragement. They need someone to talk to, someone whom they respect and who respects them. Someone who has the patience to listen and the ability to set some limits so that the mother is helped to accept her own areas of responsibility; someone who can help her to think through the situation and get support for her own impulses and decisions.

I have stated my thoughts. I am interested to know what you do and what your thinking is.

New Speaker: One thing I have noticed in developing the responsibility of the mother and that is very often the mother will lean on you even though you try not to let her do so. There will be a relationship between you two of the understanding of the child with the father left out. It is more important and I try to do it in evening hours, to have the father come back with the mother. Get him as a team on the situation.

Chairman Little: This is an excellent point. It brings the father into the picture, brings the parents together as parents, helps the child and, not to be passed over lightly, helps you by putting the load where it belongs. Do any of you have any reaction to the situation in which the mother is inconsistent in dealing with the child and when the father comes home the kids jump and behave for him?

New Speaker: I don't think that is unusual, more of the normal family life. Part of the reaction to the father is also a reaction to fear.

Chairman Little: Do you think it represents in the father a superior ability to handle the situation?

New Speaker: He has a great perspective of the child by being away most of the day and also that way has more authority over the child.

New Speaker: I think a lot of the trouble develops with the mother expecting the child to behave beyond his years. It causes more unhappiness in those who are trying harder to do the job well. It seems to me as pediatricians we can do a lot of preventive work by telling the parents at each age group what is going to happen.

Chairman Little: Dr. Gesell's books are valuable in terms of an objective description of behavior at certain ages. This is helpful but the child and the forces around him are determining factors in the behavior which he shows. The feelings which go on inside and which relate to his external behavior have never been well stated.

New Speaker: Now no matter what book is written, it is not going to apply to everybody and may be misinterpreted, unless the mother has a chance to sit down and talk over with someone who knows that there are normal variations in the thing. The printed word is dangerous in one way. I think you read those things, take them at their face value and if your child doesn't go along right by the book then something terrible is wrong. It is much better to sit down and talk about it.

(A question was raised about the difference between what a psychiatrist does and what a pediatrician can do.)

Chairman Little: I see the job of the psychiatrist as a special job of treatment of the internalized problem of the child, where the child has developed certain patterns of reaction the reason for which he is not particularly clear about. They are ingrained in his way of reading. Even though you may change almost the total environment about him, he persists in going on with this method of behavior. There are a considerable number of problems of that kind, they do need the specialized help of the child psychiatrist, and at the same time, the parents need some help with their relationship with the child. There are, however, innumerable problems of children which in a sense are reactive. The child is reacting to certain things which are hitting him now, a particular set of circumstances in his particular environment. The pattern for the behavior may come from the past

but the reason you see the behavior now is because of something happening now. If those particular circumstances can be modified in some way his behavior is going to pretty well take care of itself.

New Speaker: I think the line that is drawn depends a great deal on the individual. I come from a town of 100,000 where we have managed to get a team to work together. The social worker works with the parent and the psychiatrist works with the child. Our biggest difficulty right now is to get the child guidance clinic together with the pediatricians in town—to get the pediatricians to use them—and not only pediatricians but ministers and other people as well.

Chairman Little: Each discipline as does each individual has to learn out of its own experience its limitations. Some people in the practice of pediatrics can do an excellent job of psychotherapy. But it is not the kind of thing the average pediatrician has the time for, the interest in, or the training for. If he were primarily interested in that he would go into psychiatry.

New Speaker: One of the problems we have every day is the really spoiled child, the only child, the first child in the first year. What I would like to know is what you psychiatrists can do to educate the parents to unspoil the only child. What do you think of the idea of an educational film?

Chairman Little: Two things come to my mind around your remarks. One thing is the question of the use of educational material of that kind, which I think we might spend a minute or two on. The other thing is, what do you think spoils a child during the first year?

Speaker: Well, emotional feeling for this child is what spoils him; this child represents those feelings. The mother gives in to every whim of the child. On the problem of crying, one of the ways we get around it is to tell the mother the child has to cry a lot for the first few weeks to get good expansion of the lungs.

New Speaker: I think the help to the mother should start right in the hospital before she goes home; you can prevent a lot of those things from happening. I tell the mother that her baby is going to cry a lot during the first month. Now, during this period, especially at the beginning these cries are going to sound alike and they are all going to concern the mother so I advise her to go to the baby whenever she wants to. A little later, there is going to come a time when this baby is going to talk to the mother with these cries. Then, too, we have an hour in the morning when the mothers can report to us. That also relieves them when they know that they can report anything that concerns them.

If you ever intimate that a child is spoiled, then you are on the defensive. The mother becomes antagonistic when you use that term.

New Speaker: I think it would be an excellent idea for the obstetrician to talk to the mother during the prenatal period about these things. Also to have a psychiatrist talk to a group of mothers who are pregnant. Then a pediatrician to give a group talk too. The fathers should also be included and a pediatrician to contact the group before the mother delivers and then all along through to the meeting in the hospital; if, in that way we could develop a liaison between those 3 doctor groups, we would be doing a lot of preventive psychiatry.

Chairman Little: That is an important point. It is hard to achieve at the present time; very often it is hard to get obstetricians interested—why, I don't know, but I think it is. We are often going to be confronted with situations where that has not been done. Yet I think it is a very desirable kind of thing because mothers have a great deal of feeling as they go through pregnancy, feelings that are going to influence their reaction to their child after it is born. If some of those feelings can be met, if they can share them with somebody else, it helps a lot. The opportunity to share the feelings with another person who seems to know what we are talking about, who seems to be interested in us, can be very helpful.

Dr. Roy N. Andrews, Mankato, Minn.: It has occurred to me from these talks that every pediatrician has to do a certain amount of psychiatry. He knows the family, the mother and father; it is his duty to do a moderate amount of psychiatry and to call in the psychiatrist if the case is severe. One of the points mentioned that has been of help to me has been to bring the child in alone when he is older, that is, without the parents, and talk to him. There are many instances where you will get a lead you wouldn't get if the parents were there.

Chairman Little: That is an excellent point and one which I think a good many people do, but we often times forget to do it.

Dr. Gustavo Castaneda, Guatemala, Guatemala: Is it possible that it is unique to my experience that I have a good many children with the problem that they will not eat?

Chairman Little: It is by no means unique; I think we should bring that up for discussion a little later.

Do any of you have any strong feelings about what are the kind of things you want a mother to do in handling her child under 1 year of age?

New Speaker: Don't you think you should make the mother develop a sense of responsibility as early as possible to make it easier?

New Speaker: We have had too much of that; I think the mother should enjoy her child.

Chairman Little: I think as a rule the mother does have an adequate sense of responsibility. What do you think of saying to the mother when she raises certain questions with you, about the question of how often is she going to feed the child, for example—"What have you noticed about your child? How often does he seem to wake up? What seems to satisfy him?" Not as though you were gathering information but as though you were trying to clarify your own thinking. It helps her to realize the observations which she has made are fundamental and pretty important observations upon which good decisions can be made.

New Speaker: I wonder just how many of us do take the time to tell a mother that she is doing a good job with her child?

Chairman Little: A good point. I doubt if we do it enough although I don't think we want to lay it on too thick.

Do you feel that it makes a whole lot of difference what you feed and in general what is done to a baby during the first year of life?

New Speaker: Many babies cry a great deal through the first year of life—and we sense that this is not due to formula or allergy but have our suspicions that there are tensions in the home which the baby has picked up. We suspect that the mother is quite nervous about the baby and that may be one of the reasons it is crying and we do everything we can to reassure her.

New Speaker: I think a practical thing to do when we have a very tense mother is to tell her to pick the baby up and love it only when it is quiet; then she is apt to be more relaxed in her handling of the child. Also I like to emphasize that the mother should try to relax and not bang things continually as most tense mothers do. If they can teach themselves to relax and be slow and easy in handling the baby, it will be better.

Chairman Little: Could you put it in terms of having fun with her child when it is quiet and when it is crying to do all she can to be sure the child is all right, then if the crying continues, put it down and if possible get out of earshot—although not too far away—for a period of time? This helps the mother and gives the child a chance to go to sleep.

What place does education have in preventive psychiatry? Do you find that educating the mother, reading discussions of feeding, etc., really help?

New Speaker: If we go into teaching these people we have to keep it very simple. We are dealing with people of so many types of education, stability, etc., that you can't create just one pattern and try to teach on that scale. I think as a mother comes to you, problems will arise and can be handled at the time but I don't think you should discuss problems that might arise. In some of those cases you can create hysteria. It is the anxious kind of person who is alert to any exaggeration.

New Speaker: I sometimes wonder if a little knowledge is a dangerous thing. I don't personally advise them to buy Dr. Spock's book or any of the other books. Unless the book you recommend is in full agreement with your practice it is better not to advise this.

Chairman Little: Isn't that asking a lot of a book?

This question of education, to my mind, is very important. It has real value and it also has distinct limitations. It has to be used in terms of the individual because there are people who are anxious and who read into relatively simple things all sorts of ominous implications. It takes an awareness on our part of the people with whom we are dealing.

New Speaker: I think there is a tendency on the part of the doctor to make the mother too dependent upon him. So many of them call the doctor for every little thing instead of using good common sense.

New Speaker: I always feel that the baby is the mirror of the household. If there is a nervous mother, the child will be nervous and what you do is not so much to make the mother comfortable but to make the relationship between the mother and the baby such that the baby grows up a well adjusted child.

New Speaker: We have made a rule to allow the mother to come into our hospital and visit daily when a child is there for a length of time. When you think of it, it is cruel to take a sick child who needs his mother and put him in with strangers to perform all those tests on him. I think that is the most terrifying thing you can do to a child. Each child should be allowed to see his parents even if it does upset the routine of the ward.

New Speaker: We have instigated visiting hours in our hospitals every morning from 10 o'clock to 11 o'clock. We have found it considerable help—it relieves the nurses quite a bit; mothers help feed their children; the children are happier and quieter and the parents love it.

Chairman Little: It is my feeling that there are certain children whose parents have been tremendously protective and unnecessarily close to them and the child has a sense of relief when the parents are not there. However, there are a great many children, mostly under 6 years of age, where I think it is important for them to have frequent opportunity to see their parents. I know that those contacts will not always be satisfactory to the child, nor for the hospital personnel. It takes some understanding on the part of the nurses and the house staff of what is going on to make that contact with the parents a constructive one for the child. You have parents who are filled with all kinds of anxiety; they are going to project their difficulties on you, going to blame you for everything that is happening. They have to be directly and intelligently dealt with.

(A question was raised about preparing children for operations.)

Chairman Little: A child should be brought in about 24 hours before his operation to become accustomed to the situation, to get to know the other children and feel that this is a familiar place. With younger children—certainly those 4 years old and under—the mother should either stay with them if they are admitted very long before the operation or should bring the child in as prepared as possible just before the operation and stay with the child until he feels well or goes home.

New Speaker: One thing they have done recently at Children's Hospital in Chicago was to put the children who are not bed patients in shorts and jackets. They run around and seem a lot happier and a lot more normal. The children in bed are still in hospital gowns.

New Speaker: Does the hospital provide that or does the mother bring the clothes?

Answer: The hospital provides the outfit. They are very colorful, stripes, etc., and the children really love it.

(End of recorded material.)

Pediatrics

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SPECIAL SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

"A forum where discussion could be free, intelligent and continous."

PAUL A. HARPER, M.D., *Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

COMMUNICATION FROM DR. ARTHUR HAWLEY PARMELEE, JR.

DEAR DR. HARPER:

I read with great interest Dr. Rothman's manuscript, "The Quality of Medical Care," published in your section of PEDIATRICS in February, 1952. I am an admirer of Dr. Rothman, and his discussion of medical education was certainly a scholarly one. I would, however, like to present a difference of opinion regarding some statements in one paragraph of his manuscript. In this paragraph, he decries the fact that internes have so much time off and are getting married and having families while still in training. He infers that medical education has suffered by this change. I would like to quote some of this paragraph: ". . . at the turn of the century, the house staff had little or no time off and very little or no financial remuneration. Living quarters were provided within the hospital; matrimony was postponed . . . towards the end of the decade preceding the second world war, it became customary in the majority of the hospitals for the house staff to have every other night off, and every other week end off. Coincident with this change, the yearly stipend increased, and what with the war and some unknown factor, marriage became the rule rather than the exception. In some insidious way, the night off has recently commenced in the late afternoon. Gradually the personal life of the young physician is becoming of greater importance than his hospital duties."

The implication is that the "austere existence" of the interne whose duties confined him to the hospital and the greater amount he learned in this intensive program necessarily made him a better practicing physician than the interne who is married and has every other night off.

However, there is recently a renewed awareness that in medicine, besides the symptoms

and the physical findings of the disease, there is the patient with his fears and hopes, and with a desire for some knowledge about his condition and his future. He has also a family with fears and hopes and a desire for information. Before the patient entered the hospital, he lived with this family for some time, and after a short stay in the hospital, he will return to them. All of these people expect from the physician some kind of interpretation of the illness, and guidance for the future for the patient and themselves. This is a major part of the general everyday practice of medicine.

The young physician who has had nothing but hospital training, often concentrating on rare diseases and obscure diagnoses, finds himself quite unprepared for the office practice of medicine which he has been looking forward to. This has not only caused some difficulty in readjustment on the part of the doctor, but also some antagonism on the part of the public towards doctors. There is a great yearning for the good old family doctor who may not have made fancy diagnoses, but understood the people.

How can one balance a hospital training that is heavily weighted with the rare and obscure problem cases, with everyday living and family problems? I doubt if more confining hours in the hospital and deeper consideration of the difficult cases is the answer. Why not have a liberal combination of hospital training and family life for the trainee? The interne who sits up some night with his child at home, and sees the fear in the child's eyes, because the child can't understand why his throat hurts and his head is spinning, will have a more real understanding of the children on the ward. This same interne, who was fearful himself when he watched his sick child, and tried to reassure his wife, will have a greater understanding and compassion for the parents of the children on the ward. During his evenings at home, he will have time to contemplate and make correlations between what he has learned and observed in the hospital, and his everyday family living. Perhaps when he finishes his training, he will be the kind of doctor the public has been looking for.

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PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

MYRON E. WEGMAN, M.D., *Contributing Editor*

NURSING PLANS TO REORGANIZE

STATEMENT OF THE JOINT COORDINATING COMMITTEE ON STRUCTURE OF THE SIX NATIONAL NURSING ORGANIZATIONS

Before next fall, nursing expects to have a new national organizational structure. Instead of the six national organizations that are now concerned with professional nursing, there probably will be only two. These will be the American Nurses' Association and the National League for Nursing.

The need to coordinate national effort in nursing has been repeatedly demonstrated during the past 25 years—but never more acutely than during World War II. In spite of heroic efforts to cover essential needs and to employ practical nurses and auxiliary personnel, civilian nursing services could not hold to peacetime standards. Through recruitment, the nurse supply increased tremendously but not rapidly enough to keep pace with the phenomenal upswing in the demands for nursing service.

To make it possible for the six national organizations concerned with professional nursing to work closely with one another as well as with other groups in the war effort, the National Nursing Council for War Service Inc. was organized. This was later renamed the National Nursing Council.

After the end of World War II the council was dissolved. A joint board of directors of all six organizations was then set up. This arrangement has worked well. But the ever-mounting demand for nursing service reminds nursing that it is essential to have a more closely knit organizational structure in which nurses, allied professional workers, and other citizens concerned with nursing can move forward together with maximum speed and efficiency.

PLANNING FOR REORGANIZATION

In 1944, the boards of directors of the American Nurses' Association (ANA), the National League of Nursing Education (NLNE), and the National Organization for Public Health Nursing (NOPHN) voted to undertake a joint survey of their "organization structure, administration, functions, and facilities to determine whether a more effective means can be found to promote and carry forward the strongest possible program for professional nursing and nurses."

During 1945, the Association of Collegiate Schools of Nursing (ACSN), the American Association of Industrial Nurses (AAIN), and the National Association of Colored Graduate Nurses (NACGN) joined in the reorganization study. Although this last organization was dissolved in 1951, it is still represented on the national structure committees.

In 1950, all six participating groups voted to realign into two organizations. It was understood that one of the organizations would be the American Nurses' Association and that it would continue to be an all-professional nurse organization exclusively for pro-

fessional nurses. The other was to be a new organization for all those interested in improving nursing services and education—nurses and non-nurses alike.

ANA in the New Structure

In the new two-organization plan, the American Nurses' Association (ANA) will promote the professional, general, and economic welfare of professional nurses and help them become the best possible practitioners as individuals and as members of a profession.

Among many other activities, the ANA will:

1. Define the functions of nurses and promote standards of professional nurse practice.
2. Define the qualifications for the practitioners of nursing, including those in the various nursing specialties.
3. Promote legislation and speak for nurses in regard to legislative action concerning general health and welfare programs.
4. Survey periodically the nurse resources of the nation.
5. Provide professional counseling service to individual nurses in regard to available nurse personnel.
6. Represent nurses and serve as their national spokesman with allied professional and governmental groups and with the public.
7. Serve as the official representative of American nurses in the International Council of Nurses.

Although the ANA will be a continuing organization, a number of changes in its present structure are proposed. Chief among them are those that concern ANA sections and the House of Delegates.

The revised plan for the ANA provides sections for the following groups: (1) private duty nurses, (2) general duty nurses, (3) public health nurses, (4) institutional nursing service administrators, (5) educational administrators, consultants, and teachers, (6) industrial nurses, and (7) unaffiliated or special groups section.

ANA sections, each of which is now primarily a conference group of nurses working in a special occupational field, will have more extensive programs and much greater responsibility. Among other things, each will define the functions, standards, and qualifications for practice within the occupational field in which the members of the respective section work.

Sections in the state nurses associations will be strengthened by having proportional representation in the ANA House of Delegates—the official voting body of the members which meets every two years. At present, a state nurses association as a whole, rather than its sections, is represented in the ANA House of Delegates.

Students of professional nursing will be members of a students' council which will be affiliated with the ANA. They may take part in some general ANA activities although they will not actually be ANA members.

The New Organization

"National League for Nursing"—or, more briefly "NLN"—is the name being proposed for the new national nursing organization. When the members take necessary action, it will replace and carry forward the major programs of four of the present groups: the American Association of Industrial Nurses, the Association of Collegiate Schools of Nursing, the National League of Nursing Education, and the National Organization for

Public Health Nursing. In addition, the NLN will assume responsibility for activities in nursing never before fully developed.

The NLN will be unique among membership organizations in the United States—and, so far as is known—anywhere in the world. Through the NLN it will be possible for nurses who give direct care to patients, as well as other nurses, administrators, board members, allied professional workers such as physicians, and consumers to work together to develop and improve organized nursing services in communities, and to improve education for nursing. As a "community-centered" organization, the points of view of nurses and other citizens, both as individuals and as representatives of community health and educational agencies, will be pooled to bring about coordinated action in nursing.

Among many other activities, the NLN will:

1. Define and promote standards for organized nursing services and guide communities in achieving these standards. (Organized nursing services include those provided by hospitals, industries, schools, visiting nurse associations, health departments, and other community agencies.)

2. Promote education for nursing in all fields by defining and developing sound standards of nursing education, and guide educational institutions in achieving these standards.

3. Promote the extension and proper distribution of facilities for organized nursing service and education throughout the country.

4. Represent organized nursing services and nursing education units and serve as spokesman with allied professional, governmental, and international groups and with the public in regard to matters related to the purpose of the National League for Nursing.

5. Accredit educational programs in nursing.

The work of many national committees and services that now are jointly sponsored by two or more of the present organizations will become part of the NLN program. These include the Committee on Careers in Nursing which is working on the recruitment of nurse students, the National Committee for the Improvement of Nursing Services, the Joint Committee on Nursing in Medical Care Plans, the Joint Committee on Practical Nurses and Auxiliary Workers in Nursing Services, the National Nursing Accrediting Service, the Joint Orthopedic Nursing Advisory Service, the Joint Tuberculosis Nursing Advisory Service.

Both individuals and agencies will be eligible to join the NLN. Individual members will include professional nurses of all ranks and in all fields of nursing; members of boards and committees associated with nursing services and educational units; members of allied professional groups; and other citizens who are interested in seeing that there are sound standards for nursing service and education. Students of professional nursing will also be members, participating in a council of their own.

NLN agency members will include: nursing services organized in hospitals, convalescent homes, and other institutions; nursing services in industries, visiting nurse associations, health departments, and other community agencies; and schools and programs for nursing education whether associated with a hospital, college, or university. Collegiate schools of nursing and public health nursing units—especially visiting nurse associations—have been participating in their own national nursing organizations for many years. But it will be the first time that the other groups will have the opportunity to join a national organization dedicated to developing and improving both organized nursing services and organized education for nursing.

NLN Departments

In developing the plan for the National League for Nursing, it was recognized that attention would need to be focused on special as well as on general problems and interests. It would be essential to have not only unity but enough diversity within that unity to permit stimulation and growth of various phases of nursing.

Accordingly, the new organization will have two membership divisions—the Division of Nursing Services and the Division of Nursing Education. In the first division there will be three departments: Department of Hospital Nursing, Department of Industrial Nursing, and Department of Public Health Nursing. In the Division of Nursing Education there will be two departments: Departments of Diploma and Associate Degree Programs and Department of Baccalaureate and Higher Degree Programs.

In addition to the five departments, there will be two major types of councils—departmental and interdivisional. A departmental council will be composed of agency members within a specific department—for example, a council of public health nursing services within the Department of Public Health Nursing. In such a departmental council, agency member representatives (who will include both nurses and people who are not nurses) will be able to confer on matters that are of special interest to them, recommend to the board of directors new programs that should be carried out, and help carry forward the NLN program so far as it directly concerns that specific group of agencies. An interdivisional council will be composed of individual members who are interested in both the service and educational aspects of a special subject—such as tuberculosis, maternal and child health, orthopedic, or school nursing.

Practical Nursing

As plans for the new structure progressed, representatives of the national nursing organizations became increasingly aware that, to achieve its objective, the NLN should plan for the development and improvement of *practical* as well as *professional* nursing service and education.

Many potential NLN agency members—in particular, visiting nurse associations and hospital nursing services—employ practical nurses to help supplement the care given by professional nurses. In this way, the agencies are able to provide the community with more extensive service than would otherwise be possible in these days when there is still far greater demand for nursing care than there are nurses to give it. When considering the administration of nursing service in these agencies and what can best be done for the patient's welfare, professional and practical nursing should be considered in close relation. Also, since the service given by practical nurses supplements that given by professional nurses, the standards for practical nursing education need to be developed within the same organization that is concerned with standards for professional nursing education.

When NLN is first organized, a special committee will guide the NLN program as it relates to practical nursing. This committee will continue the work of the present Committee on Practical Nurses and Auxiliary Workers in Nursing Services which is jointly sponsored by all six national nursing organizations. Members of the new committee will include representatives of both the National Federation of Licensed Practical Nurses and the National Association for Practical Nurse Education. The groups responsible for developing the NLN plan hope that by 1953 or 1955 there will be a special department

for schools of practical nursing in the NLN Division of Nursing Education. Members of the participating organizations are now being asked to consider the advisability of having graduates of approved schools of practical nursing as NLN members. (Approved schools are those approved by the National Association for Practical Nurse Education or by the appropriate state licensing body.)

State and Local Units

Both the ANA and NLN will have state and local or district units. The ANA will continue to be a federation of state nurses' associations. Most of these state associations are divided into districts so that members may carry forward a well-developed and direct program in addition to state and national programs.

The National League for Nursing, too, will have constituent units in the states, and a State League for Nursing will have district units. It is intended that, when the members take necessary action, a State League for Nursing will take the place of any and all of the following groups that may now be organized in a state: State League of Nursing Education, State Organization for Public Health Nursing, State Association of Industrial Nurses, and a State Committee on the Improvement of Nursing Services. (The Association of Collegiate Schools of Nursing does not have state units.)

Conclusion

Realignment of the national nursing organizations will make it possible for nursing to achieve close coordination of effort and at the same time preserve the diversity which stimulates the growth of various phases of nursing.

SPECIAL ARTICLE

JOHN HOWLAND AWARD ADDRESS

By EDWARDS A. PARK, M.D.
Baltimore

INTRODUCTION

Dr. Grover F. Powers, New Haven, Conn.: Mr. President, Dr. Park, Members and Guests of the American Pediatric Society:

"What shall be done unto the man whom the king delighteth to honour?"

This regal question from Ancient Scripture is answered for this day and in this goodly company by the presentation on behalf of the Society of the first John Howland Medal and Award to Edwards A. Park!

Upon no other person could this admirable tribute of honor and respect be so fittingly bestowed. These two great leaders of pediatrics became colleagues when both were working in the New York Foundling Hospital. When Howland (1912) assumed his duties as head of the Department of Pediatrics in the Johns Hopkins University and as Pediatrician-in-Chief of the Harriet Lane Home for Invalid Children, Park joined Kenneth Blackfan there and the original Hopkins pediatric triumvirate was formed: Park, chief of out-patient service; Blackfan, chief resident on the in-patient service; and Howland, chief of chiefs! In 1921, Park moved to New Haven and became chairman of the newly organized full-time Department of Pediatrics in the Yale University School of Medicine. After six fruitful years, he returned to Baltimore as successor to those pediatric luminaries, Clemens von Pirquet and John Howland. From this post he has retired to gracious, wise and distinguished elder statesmanship—and to his microscope and slides!

I count it one of the major blessings of my own life that I have had the friendship of this first Howland laureate since I interned in the Harriet Lane Home in 1913. Such is my respect and veneration for my friend and former chief that even when I say "Ned," I actually think and feel with unabashed reverence, "Dr. Park"! In those house-staff years in Baltimore, Dr. Park "took me on," so to speak; we worked together, we talked and listened together, we walked on Broadway and in Clifton Park in quiet conversation or in understanding silence; later, there was a home, happy evenings and some pleasant baby-sitting! When he forgot his derby hat, he unceremoniously appropriated mine, microcephalic and brachycephalic though it was for him! When he lost his laboratory instrument, it was my razor which was used to prepare the guinea pig! It has been a glorious pupil-teacher-colleague experience which I mention without apology because in similar form this relationship with Ned Park has been relived over and over again by fortunate young men and women of a whole medical generation! And in this fruitful experience lies the very essence of effective education—teaching in the spirit of comradeship and by good example! Dr. Gamble has phrased it beautifully in these words: "The Park family has always managed to live in a region of trees and birds. As a visitor to this home of limitless hospitality, I recall walks in the hills behind New Haven and in the

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woods at the end of The Valley in Baltimore, in the company of students, interns and young investigators. They learned a bit of ornithology by looking through Ned's binoculars; [this] they have perhaps forgotten, but what they saw through the prisms of his personality they did not forget."

Dr. Park's career as a meticulous clinician, painstaking author, clear expositor of medicine, imaginative Red Cross and university administrator and as our foremost student of bone pathology are matters of record and public knowledge; and the breath and depth of his interest and practical concern in general medicine and its socio-economic relationships are exceeded only by his scientific achievements. But a great medical leader has other characteristics over and beyond professional competence and forensic skill. Dr. Park has many of these "other" characteristics and I wish to stress two which to me seems to possess in superlative degree—courage and generosity.

Courage, I think, is basic to all other virtues and in its physical, intellectual and moral components, Dr. Park possesses it in a truly remarkable degree. In the many years of our association, I have yet to hear him whimper or express self-sympathy in any form regarding such buffetings as life may have brought his way. If his theological forebears had all been as courageous as he is, perhaps they might have vanquished some of the old devils which still disturb our distraught world! Some years ago, he resigned from this Society on a matter of principle in face of the fact that there was at that time no other national pediatric organization which could serve as an outlet for his productive activities; later, when I asked him to accept renomination for membership he said, "Yes, but only without compromise."

In the medical socio-economic realm, Dr. Park has given imaginative leadership and is indeed a protagonist of great skill and integrity. Sir Thomas Browne once said:

"Every man is not a proper champion for truth, nor fit to take up the gauntlet in the cause of verity; many, from ignorance of these maxims, and an inconsiderate zeal unto truth, have too rashly charged the troops of error and remain as trophies unto the enemies of truth." Sir Thomas, I regret to say, did not know Ned Park who to my knowledge has never yet been a trophy unto the enemies of truth; but the intellectual field of contest is bestrewn with his opponents, particularly those who have sought to reinforce their positions with quotations from Holy Writ!

Generosity is a quality of spirit and shows itself in every thought and deed of the possessor. Generosity and the Park personality are synonymous terms whether one refers to time, personal problems, scientific projects, correspondence, hospitality, arguments. This quality was always evident in him to me but never more impressively than at the conclusion of the paper on malformations of the skull which we jointly published with, at my just insistence, Park as the senior author. This paper has been variously characterized as a "classic" and as a shining example of wasted energy: regardless of appraisal, I shall never forget Dr. Park's determination that the contribution appear as written by "Powers and Park." He assured me that it really made no difference whose name appeared first; but if in any one's mind the senior author should receive a wee bit more credit, then he wished me to receive that "wee bit" because he wanted my academic standing enhanced rather than his own!

This was at least one personal battle which I won over Ned and I report it, again without apology, as illustrative of countless experiences of Park generosity and self effacement, which could be recounted by many persons in this room and elsewhere.

No one could possibly be more considerate and kind to collaborators, friends and opponents or more interested in their happiness, welfare and advancement than he.

What I have said is but an inadequate sample of what might be recorded in very truth regarding our laureate; but the man himself, not few or many words however eloquent, justifies the action taken today by this Society.

Dr. Park, I have the special honor—which I happily share with every one in this appreciative audience—to present this Medal and this Award in memory of your friend and colleague, John Howland, as a tribute to your own rich merit as pediatric teacher and investigator and beloved friend!

Dr. McCulloch, Dr. Powers, and members of the American Pediatric Society: Dr. Powers is a dear, dear friend and has spoken from an overflowing heart. I wish that I could accept his praise as merited, but it is well that I cannot, for then I might be unendurable. To receive an honor like this, one must survive. Marriott, Blackfan, Alfred Hess, Cooley and Brenneman, as well as Howland, are gone. Think of the importance of Marriott's contribution to medicine, when together with Utheim he showed that in the infant dehydration produced the physiologic state of shock, and also Alfred Hess, when he perceived the principle that the active rays of ultraviolet light cause vitamin D to form in tissues and dead substances containing cholesterol, also Cooley's discovery of a new variety of anemia which bears his name. I am conscious that in more ways than one I have had good fortune. Will Dr. Powers and the kind friends who selected me for this great honor not think me lacking in appreciation, if I conclude by saying merely that I am very grateful?

Since this is the first time that the John Howland Award has been made and since it so happens that I have known John Howland certainly for as long as any member of the Society and, moreover, have had the privilege of a close-working association with him and an intimate friendship, I thought it might be appropriate if I put on record my reminiscences of the man. If a portrait is to arrest attention and is to survive, the subject must be made to live. Accordingly, I have attempted to portray John Howland exactly as I saw and knew him, even though I run the risk of disclosing intimacies, granted me by his friendship, which some may think should not have been told. But they are the very touches necessary to bring him back to earth and make him move and speak and act in the minds of you to whom at present he is only a name.

John Howland was born in New York City on February 3, 1873. His father, Judge Henry E. Howland of New York City, a Yale graduate, was a man of great personal charm, a distinguished citizen, and well known for his wit as an after-dinner speaker. By profession he was a lawyer and for a brief period had served as a judge, thereby earning a title, which fitted his open, genial nature well. At Yale-Harvard dinners he was pitted against Rufus Choate, who represented Harvard. Dr. Howland used to describe to me the exchange of repartée in which, as I recall, Judge Howland held his own against his celebrated and highly accomplished adversary. Judge Howland was also an extremely well-known figure in the social life of New York City, well-to-do, if not rich, and he moved in fashionable circles. But he retained a freshness and simplicity which also characterized his son. He was extremely absentminded as well as large-hearted and was so in the habit of inviting friends to dinner and forgetting to tell Mrs. Howland that it became Mrs. Howland's rule to have the dinner table always set for two or three extra guests. Dr. Howland once told me that his father loved to sit behind the family home in

Walpole, New Hampshire, whittling, while talking with his old cronies. Howland's mother was Sarah Louise Miller of a well known New York family. I recall that she was an unusually accomplished pianist. She must have been composed of the metal of which her son, John, was made, for she was once called, without warning, from the audience at a symphony concert to take the place of the solo pianist who had failed to appear and she is said to have done this with ease. Charles Howland, John's older and equally distinguished brother, once told me that it was from Mrs. Howland that the cutting edge of John's mind was inherited. I am under the impression that the immediate forebears on Judge Howland's side were solid, substantial citizens of New England—Judge Howland's father was an architect—but the Howland ancestry went back directly to John Howland of the Mayflower Company. A collateral ancestor on his mother's side was Sir William Pepperell, who led the colonists in the capture of Louisburg in 1745. Howland himself was a wonderful example of the best in New England inheritance, having a strong consciousness of duty, powerful urges toward constant improvement and complete intellectual and moral integrity. Howland spent his boyhood in New York City, at the summer home on Long Island and the Howland family home in Walpole, New Hampshire. He studied at the Cutler School, New York City, King's School, Stamford, and was finally prepared for Yale at Phillips Exeter Academy, graduating in 1890. At Exeter he was a member of the football team. He entered Yale in the class of 1894 at the age of 17. His brother, Charles, told me that he was "a hearty, wholesome boy, better than average, developing slowly and each year a little better than the year previous." At Yale he made no effort to distinguish himself as a student, though he graduated in the upper fourth of his class, but did win great distinction as an athlete and in the social life of the college. He was a member of the tennis team each of his four years, became inter-collegiate tennis champion and was elected president of the Inter-collegiate Tennis Association. He was also substitute stroke of the University crew and an editor of the *Yale News,* which in itself assured social prominence. In the senior year he was elected to Skull and Bones, the famous senior society, of which Dr. William H. Welch was also a member. It was the greatest social honor the college offered. He was in short one of the most popular and influential men in his class.

On graduation from Yale, Howland was but 21 years old and, as a tennis player, was ranked by experts sixth in the United States. He was a member of the United States doubles team. He knew intimately all the famous players of the day, Wrenn, Larned, Hovey, Hobart, Foote and the English internationalists and used to tell me most interesting stories about them. I asked him one time how he had escaped a tennis career. He replied that he realized success in tennis and in medicine were incompatible. He went on to say that he preferred to give up the game rather than not play in championship form. It is also quite characteristic that a highly practical consideration should have entered in, as revealed by the remark, "Besides I was getting too heavy." He weighed then about 180 pounds. He told me once that as a match progressed he was never conscious of the slightest fatigue and in tournament play rather expected to lose the first two sets, relying on his superior endurance in the concluding three. On entering the medical school he deliberately gave up tennis except for occasional diversion, later turning to golf.

I was under the impression that from boyhood Howland had entertained the thought of going into medicine but, according to Graham Lusk, the definite decision was made during his sophomore year at Yale. In 1895 the College of Physicians and Surgeons and the Cornell Medical Schools lengthened their required course of study from three to four years. New York University Medical School, the old Bellevue, on the other hand, still

adhered to the three year curriculum. In 1894, and indeed to 1905 when I was graduated from the College of Physicians and Surgeons, the state of medical education in the three New York medical schools was deplorable. The admission requirement was only two years of high school. Still in my time the College of Physicians and Surgeons drew its student body largely from the east side of New York City and the fashion of this type of student was to be tough and rough. In the dissecting room there were always two or three students who had tobacco pouches or wallets made of human skin, and I remember that one of them took pride in presenting one to his sweetheart. In the College of Physicians and Surgeons at Cornell, at least, there was a nucleus of college graduates of as fine a kind as was to be found anywhere, but they were in the minority, and I am not sure that such a nucleus even existed in the New York University Medical School. Howland recounted to me once how at a surgical clinic there given by Dr. Percy Bolton, an ex-Harvard crew man, the students behaved so offensively that Bolton stopped the clinic, threw off his coat, rolled up his sleeves and defied the ring leader to come down into the pit and have it out. Bolton thereafter had no trouble. Undoubtedly New York University had the lowest scholastic standard of the three.

Against the advice of his friends, among whom was Walter B. James, soon afterwards to become Professor of Medicine at the College of Physicians and Surgeons, Howland determined to enter New York University Medical School. He reasoned that all the three schools actually offered was the *degree* of Doctor of Medicine, and that by so choosing he could save one year. This decision on his part is a most extraordinary illustration of his independence and shrewdness. This instance of his behavior at the very beginning of his medical career is the key to the understanding of the man and of his successes in his later life. These same qualities can be seen coming to the surface again and again behind every move. However, on entering he took the precaution to join the famous private quiz, conducted by Dr. Ellsworth Eliot, in his office, relying on this to furnish the knowledge necessary to obtain an internship in the competitive examinations for hospital appointments toward the end of the senior year. At the end of his three years he obtained the most coveted internship, the one at Presbyterian Hospital, winning over students of four years' training.

At the expiration in 1899 of his two year internship at the Presbyterian Hospital, Howland became intern for a year at the New York Foundling Hospital. I have no idea why he happened to do this unless his object like that of others, myself later included, was to extend his experience to children. But it chanced that there Howland came in contact with the most progressive, stimulating and all-powerful personality in pediatrics at the time, Dr. L. Emmett Holt. I believe, although I have no actual evidence, that this unpremeditated association was responsible for his choice of pediatrics as a life career. Years later, after he had become firmly established at Johns Hopkins as professor of pediatrics, the chair of medicine there became vacant as the result of the resignation, followed by the death, of Theodore Janeway. Howland undoubtedly would have been given this post, had he been willing to change over. Once when I asked him why he did not do this, he replied that he was too old but added that, if he were beginning all over again, he would enter internal medicine.

After completing his service at the Foundling Hospital, Howland left for study at the University of Berlin, but soon abandoned Berlin for Vienna. I believe that Howland's first contribution to medical literature was the result of his brief study in Berlin, for in *Virchow's Archives,* volume 163, 1901, is an article entitled, "Glomerulo-nephritis bei Typhus

abdominalis" with the authorship credited to "Dr. Howland of New York." In Vienna, Howland apparently took the regular courses in pathology and clinical medicine offered to foreigners. Dr. L. Emmett Holt, Jr., reports that Howland told him many times it was this first trip to Germany which gave him the inspiration to be an investigator of disease rather than merely a successful practitioner. Study in Germany exerted the same determining influence on Howland's future associates, William Welch, Halsted, Mall and Abell. There they encountered a new kind of medicine, full of alluring possibilities, and the scales fell from their eyes.

One incident during the Vienna period should be mentioned. An Englishman by the name of Ritchie had been tennis champion of Vienna for a number of years. Howland entered the 1901 Vienna championship tournament. In the finals Howland lost the first two sets to Ritchie, but won the last three, thereby becoming champion of Vienna. The Charité in Vienna had many distinguished physicians but never before a champion tennis player. The enthusiasm can be imagined. At the Charité Howland formed with a German student, Vogt, a friendship as intimate, he told me, as any in this country. When in 1911 Howland visited Berlin, the opportunity to renew his acquaintance with Vogt was one of the special attractions. But Vogt paid no attention to his former friend although aware of his presence for weeks. Finally, near the end of Howland's stay Vogt invited him to dinner together with four Germans. Howland told me the five talked to each other as if he did not exist and that he had never felt so *de trop*. Finally, when the conversation turned to the qualities of the English, various disparaging remarks were made. But the oldest German present observed, "It is not for nothing the English climb to the tops of the highest mountains." This was three years before the first World War when pan-Germanism had been fanned to its height. Howland's feelings were so hurt by Vogt's conduct that he told me he never cared to go to Germany again.

Shortly after his return to this country, probably in 1902, Howland was made the assistant to Dr. Holt and thus definitely embarked on a pediatric career in New York City. He rose rapidly in reputation and, according to the fashion then in vogue there, accepted multiple professional positions: He became visiting physician at St. Vincent's Hospital, attending physician at Willard Parker Hospital, pathologist and attending physician to the New York Foundling Hospital and instructor and associate in pediatrics at the College of Physicians and Surgeons. He remained Dr. Holt's assistant until 1905.

In 1903, when he was 30 years old, and while still in Holt's office, he married Susan Morris Sanford, the daughter of Dr. Sanford, the leading general practitioner of New Haven, Connecticut. Dr. Sanford had been a classmate of Judge Howland at Yale and had remained a great friend. While a student at Yale, John had developed typhoid fever and Sanford took him into his own house where he was nursed until he recovered. I do not know when John's affection for Susan Sanford began, but it is safe to say that it must have been when he first saw her, for she was one of the loveliest women to look at, and the loveliest characters I have ever known, and at the same time she was made of sterling stuff. She devoted her life to her husband and gave him a beautiful home, of which she herself was the greatest ornament. She bore him four children, and he in turn adored her and shielded her from the struggle and the knowledge of the world. She exerted a great influence upon him, particularly in establishing values. When he died in 1926 it is my impression that she no longer wanted to live and she survived him only a few years.

In 1908 I first came under Howland at the New York Foundling Hospital where

he was attending physician and I an intern. The most important children's service in New York City at the time was the Children's Clinic at Bellevue Hospital. The directorship became vacant. The selection was entirely in Dr. Holt's hands. Howland was extremely anxious to be appointed. He made me his confidant, and I recall that one day he would be elated and the next depressed. When he had finally abandoned hope, he was notified by Dr. Holt that he had received the appointment.

The greatest success possible in New York City, according to the generally accepted idea of that time, lay before him, a lucrative bustling private practice with consultations and the best medical school and hospital connections. Such, however, was not his ambition. He told me at the time that what he would like most was a small hospital and laboratory service at the Yale Medical School, one which would furnish support and opportunity for study and investigation.

By this time Howland's investigative work was well under way. In 1903 he wrote on the pathologic anatomy of the Shiga bacillus infection of the intestines in infants and reported further on the subject with La Fétra the following year. In 1905 he undertook a laboratory study with A. N. Richards on the toxicity of indol and later in 1909, also in conjunction with him, the important experimental investigation of the metabolism and pathology of delayed chloroform poisoning. By 1906 the titles of his publications gave signs of definite entrance into pediatrics: A report of a case of hypertrophic stenosis of the pylorus, successfully treated by operation, possible etiologic factors in the recurrent vomiting of children and the symptoms of status lymphaticus in infants and young children. As a result of his contact with Graham Lusk at Bellevue in 1910 appeared his study on the direct metabolic measurements of healthy children during sleep. In 1908 at the New York Foundling Hospital he started with me a histologic study of the degeneration of the pneumogastric nerve in diphtheria, a study which was never published, since the results were all negative, but in 1910 and 1911 he published several papers on diphtheria. By 1910 no other young man in pediatrics in this country had shown such progressiveness and promise and it is not remarkable that he was selected in that year to be Professor of Pediatrics in the reorganized full time Medical School of Washington University, St. Louis. In preparation for this he went to Germany to study under the most distinguished pediatrician of the time, Czerny of Strasburg, then in Germany. The year's contact with Czerny had an enormous importance to Howland, since it furnished the foundation of his ideas concerning the nutritional disorders of childhood and showed him the possibilities of chemistry as a tool of research. Also it gave him the opportunity to see with his own eyes a great German clinic under a great German leader in which the advancement of knowledge was the prevailing motif.

Returning to America in late 1911, he assumed his duties in St. Louis but remained only six months. The reasons for his dissatisfaction and departure were manifold. Borden Veeder informs me that the hospital facilities and laboratories for pediatrics were grossly inadequate and although large improvements had been planned, progress was so slow that Howland felt that at least three years would be wasted waiting for them. The Howlands did not enjoy expatriation from the East, although Mrs. Howland often told me of the lovely home they had in St. Louis and her reluctance on leaving it. But the influence that must have swept all before it was the call to the chair of Pediatrics at Johns Hopkins Medical School to succeed von Pirquet who had resigned to accept the professorship of pediatrics at Breslau, Germany. This opportunity at the Johns Hopkins Medical

School must have made a tremendous appeal, since the giants of the original faculty would be his associates, with the exception of Sir William Osler who had accepted the call to Oxford some years previous.

Howland assumed his duties at the Johns Hopkins in 1912 and remained there until 1926, when he died. I shall discuss his life at Johns Hopkins in the form of personal reminiscences, but before undertaking this I should like to say a word about the illness which caused his death. In the summer of 1926 Dr. and Mrs. Howland and Dr. and Mrs. James Gamble went together to Europe. Charles Howland was then in Greece, charged with the repatriation of the Greeks from Turkish territory. The party traveled first to Greece where Charles, with all the authority and dignity of his position, received and entertained them. Gamble has told me that the tour of Greece under the guidance of Charles Howland, who was steeped in Greek history and culture, was one of the most delightful and memorable experiences of his life. From Greece the party went to France, and there temporarily separated: The Howlands remained in Paris while the Gambles toured the Basque country. While the Gambles were away, Howland was taken seriously ill in Paris. Mrs. Howland hurried him to England where medical friends awaited. Shortly after his arrival in England he had profuse gastric hemorrhages and was operated upon with the expectation of ulcer. However, the condition proved to be hopelessly advanced cirrhosis of the liver. At first Howland rallied, then had a sinking spell and died. I am glad that he did not survive, for his nature would not brook lingering illness.

DR. JOHN HOWLAND at the age of 41 years, after he had been at Johns Hopkins for 2 years.

I now come to the incident to which this account has been preparatory. While I was still in Baltimore, shortly before 1921, Howland had an attack of jaundice. For weeks his color was slightly yellow. One afternoon he asked me to feel his abdomen. He had not consulted previously any physician. I imagine that he feared neoplasm. The musculature was so powerful that I was unable to feel his liver or spleen. A few weeks later he consulted Dr. Thomas Brown who found both enlarged. Brown saw no cause for anxiety. Howland decided to give up smoking and learned the habit of chewing gum to cover the pangs of tobacco deprivation. These must have been severe. He literally chewed gum all the time when he was not on the hospital wards. I can remember him chewing gum at a pathology conference given by Dr. McCallum, when Dr. Welch was present, and the sight seemed incongruous beyond description. I do not doubt now that Howland had a viral hepatitis, not understood at the time, which smoldered into cirrhosis. I have heard the remark, "Howland must have been a tippler." He rarely touched alcohol and then, I think, only under social duress. Wilburt Davison has informed me that in the last year or two before his death Howland complained of a lack of energy and of not feeling absolutely well, but Gamble says that during his tour of Europe he was at all times in the highest spirits and overflowing with happiness, though on occasion showing fatigue.

My personal reminiscences of Howland cover the period from 1912 to 1921 with the

exception of two years when I was in France during the first World War. After 1921, my contacts with him were only occasional. My first memory, however, extends back to 1904, when I was still a medical student. Dr. Holt offered to two pairs of volunteers from the third year class the opportunity to substitute during two months of the summer at the Babies' Hospital, then situated on the corner of Lexington Avenue and Fifty-third Street. Fred Bartlett, later to become a member of this Society, who had tutored in the home of Dr. Holt's family and was a great favorite, and I were accepted as the first pair. The Babies' Hopital was then staffed with women. The superintendent, a splendid and remarkable woman, was Miss Marianna Wheeler, who though not a physician, decided on the admissions and placement of the children in the wards! Dorothy Reed, a brilliant and handsome young woman, famed for the Dorothy Reed cell in Hodgkins' disease, a great pet and worshipper of Dr. Osler, was resident; the assistant resident was Dr. Van Cholly and the pathologist was Martha Wollstein. Howland was an attending physician, though not on service when Bartlett and I were there. But he was engaged in the study of dysentery and each afternoon would come to the laboratory. His microscope, an elegant and elaborate Zeiss, was on a neighboring table under a glass bell jar. I could not restrain my curiosity. One afternoon, when the laboratory was vacant, I sneaked over, took off the bell jar and had just accidentally dipped the high dry lens into a drop of cedar oil, when I heard Howland's voice in the hall. I barely had time to get to my desk and appear absorbed, when he came in and sat down. Presently the dreaded words—"Someone has been using my microscope." I became still more absorbed. From other parts of the laboratory came—"I haven't." "Well, someone's been using it," Howland repeated, but did not put me to the test. Perhaps he suspected only women.

I gained the impression that the women there disliked Howland. As I recollect, his hair was beginning to thin on top even at that time and it was cut not more than one-quarter inch long. I have heard the women refer to him as "the convict." His arrival was often announced by, "Here comes the convict." Howland never approved of women doctors. He believed, like Milton and most men, that the place of a woman is in the home. I have heard it said that he must have had some unpleasant experience to explain so strong an aversion. This may well have been at the Babies' Hospital at that particular time though I hasten to add that he came to respect and like women members of his staff, in particular Katherine Dodd and Margaret Handy, and as he grew older, this early attitude showed signs of mellowing. But I recall once when walking along the ground floor corridor of the Harriet Lane, the door to the interns' lounging room swung open and there was the lone woman intern, Catherine Creighton, sitting on a table, not so lone, with feet swinging and blowing out a cloud of smoke. Howland clutched me by the arm saying, "Did you see that?" He could not stand women smoking. He once gave my sister the compliment, "She has a mind like a man."

As already remarked, I first came under Howland in 1908 at the New York Foundling Hospital. When I left there, I studied pathology at the City Hospital, Welfare Island, for five months and then became office assistant to Dr. Theodore Janeway, who was Professor of Medicine at the College of Phyicians and Surgeons. Having become interested in rickets at the New York Foundling Hospital, I had gone to Germany in the summer of 1912 to study the pathology of that disease under Professor M. B. Schmidt in Marburg. One day I received a cablegram from Howland offering me a post of assistant to him in pediatrics at Johns Hopkins. Since I had contracted to stay the ensuing year with Janeway, I

declined. Janeway, hearing and realizing the situation, with great generosity cabled me a release and advised me strongly to accept Howland's offer which I did.

I returned to this country in September of 1912 and repaired at once to Baltimore. When I arrived at the Pennsylvania Station, there was Howland waiting for me, wearing a straw hat. We boarded a street car and he gave me my first glimpse of the Johns Hopkins Hospital. When I was a student at Yale, I remember passing through Baltimore. I had to wait an hour for my connection at the Pennsylvania Station and, thinking that I might get some idea of the city, issued forth. In front of the station a mule had been caught in one of the large rope nets, the species of cow catcher, with which the street cars were then equipped. I stood for half an hour in the rain, watching the Negroes trying to extricate the mule, poking and whipping, but nothing seemed to interfere with the animal's contentment and complacency. After considerable time the mule was pulled out, traffic resumed and I took my train. How little did I think that my own future would be cast in Baltimore! I shall now speak of Howland, first professionally and then as a man, attempting to picture him exactly as I saw him.

When Howland came to Baltimore as Professor of Pediatrics, there was no pediatric department. Von Pirquet had been professor from 1910 to 1911, but had no hospital building. He had been obliged to work in a couple of rooms assigned to pediatrics in the medical dispensary. It was he who had designed the building of the Harriet Lane Home on the basis of some pre-existing plans. In 1911 he returned to Germany on leave of absence and, while there, accepted the chair of pediatrics in Breslau. In 1912 when Howland arrived, the Harriet Lane Building was completed. Howland's task was to organize his department.

Howland brought Kenneth Blackfan, who had been his resident in St. Louis, to be his resident in the Harriet Lane. Blackfan had been doubly recommended to Howland by Richard Pearce in Albany, and David Edsall in Philadelphia, under both of whom he had worked. I was placed in charge of the dispensary. There were three interns. I recall vividly the opening day of the dispensary, much heralded and important to us; there were 16 patients. There was money enough for the operation of only one ward floor, but this was rapidly filled with sick children. Howland's staff soon grew, as it became known that a new kind of clinic was being organized at Johns Hopkins under this brilliant progressive new kind of young man, aiming at goals higher than merely preparation for medical practice. McKim Marriott, released by Borden Veeder, when Veeder had to leave on account of his health for Saranac, came in 1914, Powers was intern in 1913 and remained, a bulwark of the department, until 1921 when he left to go with me to New Haven. In 1915 Gamble and Warren Sisson, attracted by the new opportunities, joined Howland's staff. Alfred Shohl also came that year. In 1916 Marriott left to become Professor of Pediatrics at Washington University, taking Samuel Clausen, an intern of great promise, with him. The following year Benjamin Kramer took Marriott's place. Frederick Tisdall arrived in 1918, sent specifically to the Harriet Lane from Toronto by Dr. Alan Brown, in order to obtain a foundation in pediatrics. Wilburt Davison and Horton Casparis came in 1919 and Graham Ross in 1920.

I do not believe that Howland ever thought out the organization of the Department of Pediatrics; rather it was an unconscious development. If there ever was a "one man department," it was Pediatrics under Howland at the Harriet Lane Home. He took sole care of the children on the wards. He also took charge personally of all the private

patients. He used to do certainly two-thirds of the teaching and of course all the administration. Few could have done all this but he swung the load easily. There was a sharp division between the clinical staff on the wards and the laboratory men. Howland did not want his resident staff to have any duties except the care of the children and always demanded that at all times they be at his beck and call. Later, when Blackfan relinquished the residency after seven years, his place was taken by William Happ. Happ had worked with Moss in establishing the Moss classification of the blood groups. Happ was an investigator by nature and was interested in extending studies of the blood groups to the newborn. Whenever he had the opportunity, he sneaked off to the obstetrical ward or to the laboratory. I can remember when Howland would arrive on the wards exclaiming, "Where's Happ?" He never liked Happ as a resident because Happ would not be "the boy on the burning deck."

Howland's organization of his interns was interesting. They were assigned in rotation the children admitted to the wards, but they also worked in the Dispensary. The important point in the arrangement was that when a child was discharged to the Dispensary his doctor on the wards took charge of him in the Dispensary. Thus each intern had his own group of patients, bed and ambulatory, just like a practicing physician, except that he did not make home visits. Each intern also did all the laboratory work required, including bacteriology. The arrangement was ideal, for it gave the intern an understanding of his patient as an integrated whole and it also cultivated the doctor-patient relationship. The interns became greatly interested in their patients as individuals and the patients in their turn loved to come back to their doctor in the Harriet Lane. The plan was only possible because the Harriet Lane service was so small. But it was in such contrast to the present system, in which division of labor makes it necessary to piece together the perspective of the child from charts and sheets of data and the personal relationship goes by the board. In Howland's clinic the personal touch was kept in all its purity.

When Howland was away, in particular during his summer vacation, Blackfan had entire charge of the wards. This was in accordance with the Johns Hopkins residency system which Howland adopted in all its details. But it could not have been otherwise, for Blackfan was by far the best physician in the department and fashioned medically in Howland's own image. The research staff were allowed to work in the dispensary but were not given ward privileges. Marriott was so essential to Howland in the laboratory that he had the greatest difficulty in obtaining consent even to work in the dispensary. The same situation developed later in Kramer's case. Both had fairly to force their way. I was in a somewhat different situation. I was free to work in the laboratory, as soon as my dispensary job, which took only one-half day, was over. In 1916, Howland replaced me in the dispensary by Powers and I became a full time research worker without any clinical outlet.

I used to think that Howland's method of organization of the department was not the best for its fullest fruition. We underlings were never allowed experiences essential for the development of ideas and we had no opportunity to carry out the ideas which we did have. With the exception of a clinic for the treatment of congenital syphilis, Howland would not allow any special clinics or the formation of any subdepartments, but the organization had great advantages, particularly for him. His policy kept the department small and completely under his immediate control. He was able to spend every afternoon in the laboratory. How many department heads are there who have not relinquished

their own investigative work because of the accumulation of other duties, the development of which was in many instances merely an expression of size! Moreover, Howland's system was particularly conducive to successful research for all the rest of us. We were able to concentrate virtually all our time and attention on our problems. When Theodore Janeway resigned the chair of Medicine at Johns Hopkins, he told me that he had two choices: One was to distribute experience and responsibility for the care of patients among the staff and for himself to become an administrator; the other to assume all the clinical responsibilities himself. The former, he remarked, he would not do, and the latter he could not. But Howland followed the second alternative. The reason that he did not divide clinical responsibilities lay, I believe, in his conscientiousness. I have never known any physician who felt his responsibilities toward his patients more keenly. He could not rest easy unless he himself saw with his own eyes what was going on and knew it to be right. In my last two years he assigned me for a time to the wards, but the resident staff paid no attention to my orders. They knew that Dr. Howland would always happen up later and waited for him. Later, I am told, Howland gave Davison and Kramer some real ward responsibility. The bulk of the teaching Howland did because he loved it so, although he would have denied this.

As a clinician Howland had few peers. His diagnosis was either correct or as close as possible to the truth. In arriving at a conclusion he brought to bear an immense, accurately remembered experience, a wide and exact knowledge of disease which increased noticeably when he became with Dr. Holt a joint editor of *Holt's Diseases of Childhood* and a shrewdness which cannot be overemphasized. He had the kind of memory, often possessed by great clinicians, which enabled him to recall the name of the child, the time when the child had been a patient and the bed occupied in the wards. He had the shrewdness of a master horse trader. Only on one occasion did I ever see him make what I should call a complete physical examination. He would listen carefully to the history, ask questions and then examine the child in the pertinent places. He never lost the perspective in details. I think I have known other clinicians who were more sensitive to nuances, but never one who day after day would have a higher average score. As a diagnostician, consciousness of himself or emotion never got in the way of his judgement; he was never afraid to say that he did not know and never felt impelled to take chances in order to show brilliance or superiority. He was at his best, the greater the difficulties. Therapeutically, he was conservative and his sound judgment certainly caused him to make few mistakes. He realized fully the value of waiting for time to make situations clear. He never did anything or allowed anything to be done which by any remote possibility could injure a child. He understood children and his relations with them were delightful to watch. At will he could meet a child on an equality; children at once trusted him. He taught me, when examining a terrified child, always to look the other way.

In the days when I was with Howland the problem of infant feeding was perhaps still paramount in pediatrics. His views were a mixture of those of his two great teachers, Holt and Czerny. He used an exclusive protein milk diet for the treatment of diarrhea and also for celiac disease. In celiac disease after some weeks he would add a half ounce of cereal and all, he included, trembled in fear of the result. Toward the end of each summer the wards would become filled with celiac disease. In retrospect I feel sure that most of these were examples of Czerny's *milchnährschaden*, created by an exclusive pro-

tein milk diet. I believe that, after I left, Howland used to add two and a half per cent sugar to his protein milk but with some doubt in his mind. When a child vomited, he used to follow the teachings of Holt and first dilute, then take out the fat, and then, if necessary, the sugar. In this country it was Marriott who first perceived that the difficulties in infant feeding were largely created by the mistaken ideas and rigid attitudes of the pediatricians themselves. When I visited Marriott in 1920, he remarked, "Infant feeding, there's nothing to it." Of course there is a great deal to it, but it is not what we formerly thought. The skill which is required is not that of science but of the gardener who knows all the little things necessary to raise a tender plant.

As a teacher Howland was superb and I believe that he was generally regarded by the students as the best teacher in the Medical School and was terribly dreaded. But they would not have dreaded him, had they known how kindly he was within. Students were assigned in pairs to patients whom they were expected to study the night before. Howland used the Socratic method, developing the case by asking questions. In this way he best accomplished the result most desired in all teaching, namely, making the student think. I always attended his clinics and almost always learned something new. I used to think that these clinics were the best of my experience. It was his habit to show successively 4 or 5 patients. He said to me once that he thought it to be a great mistake to go into a case exhaustively, for what the students remembered were a few things which they saw with their eyes or learned by feeling with their hands. The clinics which I have just described were Howland's informal ones. His formal clinics, in which he presented patients in illustrated lecture fashion, were not so good. In regard to these formal clinics he showed, strange as it may seem, a certain insecurity and quite regularly used to ask me afterwards how I thought the clinic had gone, sometimes throwing out a remark that it was "terrible."

I should have added that he never showed cases to the students when the diagnosis was not clear. He demanded either that it be proved or so nearly certain that an error would be unlikely. I recall, however, an occasional mistake and twice, when he showed a baby as having tuberculous meningitis, a lumbar puncture, performed before the students, yielded a cloudy fluid.

When Howland wished to give a clinic on a subject in which some member of the department had special knowledge, he used to call him into his office and discuss the subject at length with him. He relied particularly on picking other people's minds as a means of keeping abreast with medical knowledge, and made use of it whenever occasion offered.

When I was a student at the College of Physicians and Surgeons it was believed to be the duty of the teacher to cover systematically his entire subject in the course of the year. Dr. Holt, for example, gave us seriatim definite assignments of pages in his book, so that by the end of the term the entire book had been read. Howland's teaching of pediatrics, in contrast, was completely unsystematic. With the exception of infant feeding and nutrition, which was taken up systematically in the form of lectures by his assistants, the conditions presented to students depended entirely on the cases which happened to be in the wards. If a certain disease never was represented, it was not taught. This haphazard method of teaching pediatrics troubled me, when I first joined Howland's staff. But I soon learned to appreciate that the important object to be obtained by the teacher is not the transfer of facts but to show the students how to think. If he learns how to organize his mind so as to approach a medical problem effectively, the acquisition of the facts of a given disease is a simple matter. It should be remarked, however, that the cases in

the Harriet Lane wards occupied a very wide range, so that the omissions were not great.

I must not leave the discussion of Howland as a teacher without mentioning one or two of his special delights. He loved to open with his forefinger, the nail of which was pruned to a point, retropharyngeal abscesses in both his major and minor clinics and children with this condition were always saved for his clinics, if possible. Indeed, except in extreme circumstances no member of the staff ever opened a retropharyngeal abscess on the wards because of the known thrill Howland got out of doing it himself. Howland also loved to intubate and extubate and children requiring this were held over for him and in particular for his clinics, whenever it was safe.

He was a remarkable example of the unconscious teacher, the teacher, I mean, who does not know that he is teaching. He made us all try to be like him.

As an investigator Howland was an opportunist, as almost all clinicians are obliged to be. In general he chose subjects for his studies in which from the beginning he could see the end. I have often heard him remark that he had a good paper for an approaching meeting. The subjects chosen for his earlier studies appeared to be as chance offered, but later, when he became interested in rickets, they had a continuity, one leading to another. But he was extraordinarily keen in perceiving possible openings and a superb judge of their value. In his studies with the calorimeter he worked alone, but almost always it was in collaboration with someone else. The collaborator might be chosen because his problem appealed particularly to Howland, but more often because of the possession of some special knowledge or ability which Howland did not possess. A. N. Richards was an early collaborator and in general it may be said that the collaborators whom he chose were most unusual men. His later work was done chiefly with Marriott and Kramer. I believe that Howland did not have what might be called an imaginative or creative mind; I used to think that he was unusually dependent on others for ideas. The great asset which he possessed, and its importance cannot be overemphasized, particularly as a department head, was his almost unerring judgment. As already said, he early perceived the importance of chemistry for the investigation of disease in children.

Dr. Howland did not provide technicians in the chemical laboratory. He insisted that the investigator must gain thorough experience and resourcefulness in the use of the required methodology in order to have full faith in his results. Although he had little knowledge of theoretical chemistry, he was remarkably skillful in technician procedures. He admired their ingenuity and enjoyed the challenge of attainable accuracy. Shohl used to say that Howland was the best "spinal cord" chemist he had ever seen. He had another objection to the employment of technicians: He once said to me that departmental money was more wisely spent on staff members than on technical assistants since only in the former lay the possibility of creative work. However, he made an exception in my case and allowed me to have a histological technician.

As already indicated, he chose subjects for investigation with great intelligence and insight as well as judgment. He was extraordinarily wide awake. Czerny had expressed the opinion that in the children suffering from diarrhea and dehydration an acidosis existed. Watson Sellards, I think inspired by Howland, had already found indication of this by means of a crude indicator test. Howland's first great accomplishment in the Harriet Lane was the proof that an acidosis existed in these children. The selection of the problem chosen was Howland's, the development of a method for the recognition of the acidosis was Marriott's contribution.

I now digress to decribe a most gallant act. Oscar Schloss in New York City had also

demonstrated acidosis in these so-called "intoxicated" children. Learning of Howland and Marriott's work, Schloss wrote Howland saying that he would defer his report until Howland and Marriott had published theirs. This he did. It was an act of courtesy and generosity from a younger to an older man which deserves unstinted praise. Actually I think Schloss saw farther into the problem than did Howland and Marriott, for he recognized that the primary disorder lay in the inability of the kidney to perform its regulatory function.

William G. McCollum and Vogtlein had shown that in the tetany following the removal of the parathyroid glands the calcium in the blood serum was low. Howland and Marriott determined to see whether the calcium was also low in the tetany of infants. They found that it was and went on to develop a successful treatment of the convulsions through the administration of calcium. Here again, Howland's mind was the one which seized upon the opportunity. In 1918, when I was in France, during the First World War, I received a cable from Howland stating that McCollum had just shown him rats with skeletal changes which he believed were those of rickets. The message ended by urging me to come back to this country as fast as I could. Sherman and Pappenheimer in New York and McCollum, Shipley and I showed that rickets could be produced in the rat through diets which were deficient in phosphorus. I think that this discovery had a particular importance because previously all thought in regard to the disease postulated that the metabolic defect lay in the calcium. Howland, and I do not doubt Kramer equally, saw that the time had come in rickets to determine the complete electrolyte pattern of the blood serum. This they were able to do as the result of Kramer's mastery of the micro-chemical methods, with the result that the blood serum was found to be deficient in inorganic phosphorus. The idea that the product of the Ca $\times$ P of the blood serum is an index of rickets was Kramer's. I think that this fundamental discovery that rickets in the child is characterized by a deficiency in the serum inorganic phosphorus, a discovery made at the same time by two Danes, Iverson and Lenstrup, ranks first in importance among Howland's contributions, in the glory of which of course Kramer shares. Howland made numerous other important additions to knowledge but the ones I have mentioned are the most outstanding. At the time of his death Howland was preparing to work with Shipley on the factors involved in *in vitro* calcification.

I cannot think of an instance in which Howland assigned a problem to any of us. We chose our own and he never interfered in our prosecution of them. He never pressed us to publish. He remained so completely engrossed in what he was doing that, I think, he was unaware most of the time, unless we especially told him, how our work was going, but he was always interested to know and always offered sound advice.

As an administrator of a department Howland never seemed to administer. His grasp of things and his judgment were so accurate that he made the right decisions immediately without effort. Administration would be reduced to a simple process for all of us, if situations were always clear and actions evident. Moreover he understood people. Of course Howland was greatly aided in keeping administration at a minimum by keeping his department small.

But Howland hated quarrels and disagreeable personal encounters and dodged them whenever he could. The supervising nurse of the Harriet Lane had been a pet of von Pirquet and had been given great authority by him and perhaps spoiled. In addition she was an ardent feminist and, anathema to Howland, carried banners in feminist parades! Howland

and she clashed almost on the first day. Crowds of nurses suddenly inundated the building, making a hubbub and noise. When Howland protested, saying that his permission had not been granted, I heard Miss M. reply, "Dr. Howland, this is their home." But Howland left most of the battle to Blackfan and me. When we approached his office to report, Howland's door would open a crack, his head would pop out and he would say in a loud whisper, "How did you get along?" After the supervisor left, I continued the warfare with her successor, Miss S. The only occasion when Howland ever reproved me—and the need was great—was when he called me to his office and asked me to stop because, as he said, he "could not stand it any longer." I might add parenthetically that Blackfan made numerous attempts to heal the wounds between Miss S. and me and with his tact and general human understanding would begin, "Ned, Miss S. just thinks the world of you"—the significance of which depended on one's definition of the world. I recall once Howland told me that he consented to have his number 2 secretary, with whom I had to work and who was perfectly terrible, discharged, if I would do the discharging. This I finally succeeded in doing, but the difficulty in making her understand that she was to leave was quite as great as making the mule caught in the net of the street car realize that the time had come for him to get up and go.

As an administrator, and indeed in all aspects of his life, Howland showed a most amusing thrift, mixed with much generosity and large mindedness. Dr. Weed, the Director of the Medical School, told me after Howland's death that each year he turned back a considerable unexpended budget—this although we were, or at least thought we were, on the skinniest salaries. At the end of each year he could not resist buying quantities of glassware from A. H. Thomas and Company at their annual bargain sale. When I returned to the Harriet Lane in 1927, I found a whole storeroom in the basement filled with it. When Gamble was called to Boston by Morse, Howland remarked, "Go up there and find out how much salary Morse offers, and I will give you the same."

Once when Howland was leaving for the summer, he said to me that he would like to have me come and stay at his house, where I would be cool and comfortable. I was happy where I was and did not want to go and indeed knew that the arrangement would be inconvenient, for the nearest restaurant was at the Pennsylvania Station a mile and a half away and by street car. But I felt obliged to accept. When I appeared, just before his departure, he presented me with a loaded revolver and a loaded cane, saying that I could keep them under my pillow. Up to that time it had never occurred to me that any danger existed. One evening when I returned quite late, I found a light burning in one of the rooms. Assuming there was someone in the house, I took the revolver in my right hand and in the left the loaded cane and in addition a lighted candle and proceeded to make a search room after room. I do not know what would have happened if I had encountered a burglar. I remember that with my hands so full I had great difficulty in opening the doors. It turned out afterwards that a servant had visited the house and had left the light burning. I believe that Dr. Powers took my place as a much more efficient guardian the following year.

In discussing Howland as an administrator his attitude toward new ideas should be mentioned. When a suggestion was made to him, he often seemed to reject it or to be uninterested; then perhaps after a month or two he would present it back as his. The idea to be accepted had to be assimilated. When this happened, we were all sure that he had no recollection of its source. This habit of his used to give us all great amuse-

ment. In regard to new ideas, particularly if they involved changes in policy, his conservatism showed itself strikingly. Especially in infant feeding he demanded that proposed changes be tried before they could be accepted and this meant that the trial had to be elsewhere. I think that this extreme reluctance to depart from the accustomed held the Harriet Lane Home back in later years. He was extremely receptive to suggestions in the research field, however.

I should now like to speak of Howland's feelings in regard to some of his teachers and then of his feelings and relations to some members of his own staff. Since Howland was the personal assistant of Dr. Holt for several years, his opinions concerning him have the special value of most intimate experience. A number of times Howland said to me, referring to Dr. Holt, "His mind is as smart as a steel trap," and I never heard him apply the figure to anyone else. To one who knew Dr. Holt the comparison has an immediately understandable significance which is, however, hard to explain to those who did not know him. He also said to me on several different occasions, again referring to Dr. Holt, that "his deed was better than his word." He also expressed the opinion to me more than once that he believed Dr. Holt to be a greater man than Sir William Osler. I never heard Howland make a single adverse criticism of Dr. Holt and it is evident that his admiration for him was unqualified. I know that he felt greatly indebted to Dr. Holt for giving him his start.

Dr. Holt was famous for never expressing praise. To anyone who has read his biography it becomes clear that the most intense feelings of affection and gratitude burned within, but could never find expression on account of his inhibitions. Howland told me that he was once sent by Dr. Holt to see a little girl whom Dr. Holt had examined a day or two previously and had thought was suffering merely from a digestive upset. On arriving at her home and making an examination Howland concluded that she had appendicitis with abscess formation. On being notified by Howland of his opinion Holt hurried to the house and confirmed the diagnosis. As the two walked down the front steps, Dr. Holt remarked, "Well, doctor, it pays to keep your eyes open." Howland told me that this was the closest approach to praise he had ever received from Dr. Holt.

Howland also had a great admiration for the German pediatrician under whom he had worked in Strasburg, Czerny. Howland told me that Czerny's knowledge of pediatrics was encyclopedic and that he was able to give a clinic or a lecture on any subject in pediatrics without any previous preparation. When Czerny was about to give a clinic, he used to call out to his assistant, according to Howland, "What is there this morning?" His assistant would reply, "I have a child with such-and-such a disease," and Czerny would walk into the lecture room and expound. The Harriet Lane must have resembled Czerny's clinic in Strasburg in more than one respect. Ludwig Meyer once told me that Czerny himself worked late into the night in the chemical laboratory and that throughout the clinic there was the spirit of enthusiasm and suppressed excitement.

Howland had a great admiration and affection for Dr. Graham Lusk of New York City. I cannot recall that I ever heard him mention or express any opinion about his other colleagues or teachers in New York City.

Howland had a great admiration for Blackfan and was extremely fond and proud of him and at the same time greatly amused by him, but always regarded him as a subordinate. He was never able to overlook the fact that Blackfan had never had a uni-

versity education. But I think that Blackfan himself cultivated this attitude. For example, Blackfan realized that Howland loved to make the diagnosis himself. How often on rounds did we witness Blackfan, when he knew as well as anyone what the diagnosis was, recite the symptoms and physical signs in such a way that Howland would suddenly exclaim, "Why, Blackfan, this child has meningococcal meningitis." Blackfan greatly enjoyed the success of his guile. As an illustration of Blackfan's tact with his chief, I give the following instance. I was sitting beside Howland at his desk in his office, while he was painstakingly correcting McClure's and my paper on the results of extirpation of the thymus gland, sentence by sentence. I should here mention that Howland spent hours and hours with us over our papers and in one instance he largely rewrote mine. There was a knock on the door and Howland, without looking up, called out, "Come in." The door opened a crack and Blackfan stuck his head in, saying, "A woman, a private patient, has just come with her child to see you." Howland, still without looking up said, "You take care of her, Blackfan. I'm too busy." Twenty minutes later there was another knock at the door and Blackfan's head again appeared. Perceiving that Howland was still completely engrossed in the manuscript, Blackfan gave me a "half-side of the face" wink and said, "Dr. Howland, she has come all the way from California and she thinks you're the greatest doctor in the world." "Show her in," said Howland. Do not get for a moment from this the impression that Howland was conceited. He was not; he was just like the rest of us. The doors to his innermost nature were wide open and when one walked in and looked around, everything was neat and fresh and clean. The difference between him and us was that in him natural responses were not concealed.

Blackfan had a great natural curiosity and longed to go into the chemical laboratory and to learn methods and to work there. But Howland's policy toward his resident prevented this. Howland found Blackfan and made him and Blackfan's over-all debt to Howland was tremendous, but Howland's restriction prevented Blackfan from flowering in yet another direction in the formative period of his life, for he had the potentiality of a splendid investigator. By the time Blackfan had completed his residency, we all had the impression that as a clinician he was fully equal to Howland.

I am under the impression that Howland advised strongly against making Blackfan Professor of Pediatrics at Harvard. He said to me once, that, in taking Blackfan, Harvard was making a great mistake. Howland had made all the arrangements for Blackfan to go into private practice in Baltimore, when the Cincinnati call came, and I believe that Blackfan himself had made preparations to do so. They say that a man is never a hero to his valet; probably it is also true the other way around, witness The Admirable Crichton. When a man forges ahead in medicine from a very poor start or against great difficulties, it is a good rule to look out for him. I think that Blackfan was the ablest head of a department of pediatrics of all of us. He, too, was cut off in his prime.

Howland had an enormous admiration for Marriott, as indeed all the rest of us had. There was a good deal of the magician about Marriott, both natural and cultivated. Everything was easy; nothing was impossible. In the chemical laboratory Marriott was able in one way or another to meet Howland's every wish, often by the following morning. Howland would point out the problem, Marriott would develop the method to solve it, for example, his colorimetric method for the measurement of the pH of the blood serum. Marriott was a big man with prominent eyes, a florid face and high-

pitched, almost falsetto, voice. In their general outlook on life Marriott and Howland were in strong contrast. Marriott was what might be termed a belligerent pacifist; Howland was vehemently pro-British and most out-spoken in the belief that our entrance into the war against Germany was not only necessary but right. I can hear now the acrimonious discussions across the broad soapstone top of the chemical laboratory table interspersed between measurements. Howland tried to prevent Marriott from going to St. Louis. He believed that Marriott had not sufficient clinical training to be a competent head of a clinical department. As a matter of fact, Marriott's previous clinical experience before coming to the Harriet Lane had been limited to two summers when he was the official physician in Yellowstone Park. He was fond of asking what were the two commonest ailments in Yellowstone Park which he was called upon to treat. The answer was "bear bites and geyser burns." But Howland had immense regard for Marriott. Once when in a moment of discouragement I happened to compare myself with Marriott, Howland remarked, "You must not be governed by Marriott; he is an exception."

In a way it is too bad that Marriott and Howland were ever separated. They made a wonderful combination; Marriott had the imagination and the ingenuity and Howland supplied the balance. When later Marriott entered the clinical field, with which he was not sufficiently familiar, he made some bad mistakes, which Howland's judgment would have prevented. But under Howland's restraining influence Marriott would never have been allowed to soar and exert his revolutionary influence in debunking infant feeding.

Howland was enormously indebted to Kramer and I think that Kramer's contributions to pediatrics have never been adequately appreciated. Kramer's mastery and development of micro-measurements for the electrolytes made the analysis of the blood for them possible. Howland parted with Kramer with the greatest reluctance.

James Gamble was the beloved disciple and Howland's particular companion. Gamble used to stop each morning on the way to the Harriet Lane at Howland's house in order to bring him to the hospital. Gamble would arrive at the appointed time, half past eight, and quite regularly Howland would appear at the door exclaiming, "Wait, Gamble, till I have had a cup of coffee." Gamble would go in and find that Howland had not yet sat down to breakfast. I think that Howland was devoted to Gamble as to very few, but never realized his potentialities until Gamble had left him and gone to Boston and the work on the metabolism of starvation in children, done in collaboration with Ross and Tisdall, was published. Gamble has told me that Howland could not understand his decision not to work in the Harriet Lane dispensary and definitely to abandon the idea of being a clinician. I think that Howland thought that Gamble's chosen course meant failure in life. He believed that a man must head either for clinical medicine or for the fundamental sciences and that an intermediary position was totally impractical. After Gamble had gone to Boston Howland made a determined effort to get him back. But Gamble had by that time become firmly rooted.

I believe that Howland was never able to decide whether Alfred Shohl had ability or not. Shohl amply demonstrated his worth subsequently by his studies in rickets. I well recall Howland's and also Marriott the pacificist's wrath when Shohl, who worked at night, took apart a hydrogen ion electrode apparatus which Marriott had set up with great difficulty, just to see how it was constructed, and could not get it together again by morning.

Howland was slow in appreciating Powers but ultimately completely realized his value.

I was what might have been called the "pinch" teacher of the department. I recall one time when Howland's secretary telephoned me to come over immediately from the Hunterian Laboratory and replace him in his clinic. He had been called to an urgent faculty meeting and would leave the moment I arrived. When I appeared in the amphitheater, he whispered to me what he thought the patient had and repeated in my ear his last sentence to the students. The situation was so amusing to all concerned that the remainder of the clinic went very well. He said to me afterwards that he would never do that again.

I was downed by him in diagnosis on numerous occasions, the mortifications of some of which still live in my memory. But I had one triumph. He used to go on the wards about four o'clock in the afternoon on the day before his clinic in order to select cases. When he could not find an interesting case, he often said, to the great amusement of his junior staff, "Get Park to teach." On one of these occasions I hastened to the wards to find a suitable case. The only possibility seemed to be a baby who had been in the wards for several weeks with an unexplained fever. I determined to present the case as a diagnostic problem. On going over the child carefully I noted a hyperesthesia and increased tendon reflexes without a single other clue. I asked for a lumbar puncture and presently one of the interns rushed over to the Hunterian with a test tube in his hand, showing a cloudy fluid in which there were meningococci. The afternoon after the clinic I happened to meet Dr. Howland in the hallway. He stopped me saying, "Do you know what that child with the unexplained fever has? He has meningococcus meningitis."

Howland's special interests, apart from medicine, were as clearly defined as everything else in his character. Probably because of his own athletic ability and training he was greatly interested in certain sports. One particular interest was track events. Several times he took me to see intercollegiate track meets and commented on the form of the runners as they passed by and guessed the winner on the basis of form. Twice he took me to see marathon races. One of them was won by a Frenchman, named Jean St. Jean, who excited his admiration because of the ease of his stride. Strangely enough, he did not seem interested in the national and Davis Cup tennis tournaments, not nearly so much as in the golf tournaments. He persuaded me to go with him to watch the famous professionals, Vardon and Ray, in an exhibition match at the Baltimore Country Club, although I had never played a game of golf in my life. We followed the players from hole to hole and Howland kept commenting on their form, strategy and shots. In regard to Howland's golf and his golfing excursions James Gamble has written most entertainingly.

"Dr. Howland was the most ardent golfer I have ever known. He played not by the round but by the day. If after 18 holes in the morning and again in the afternoon, there was daylight left, he would play some more. My only rigidly prescribed assignment in his department was to play with him on Sunday mornings as a tuning-up exercise for the afternoon foursome which was the event of the week for him. I was not good enough to participate in this foursome.

"In the year 1915, I got my first car and this greatly extended our golfing operations. Dr. Howland became a non-resident member in the newly developed Pine Valley course

in New Jersey between Philadelphia and Atlantic City. It is a very beautiful and difficult course with a pleasant dormitory to spend the night in. We often went there for a few days, taking along, as a pretext, laboratory data for contemplation. We never looked at them. Our most memorable visit to Pine Valley was en route to the meetings of the American Medical Association at Atlantic City. We set out on a Friday afternoon, and according to plan played golf all day Saturday and Sunday. It was lovely June weather. We were to move on to Atlantic City Monday morning. But it was a very beautiful morning. Dr. Howland got out his program and after careful study of it announced that there was not a single paper in any of the sessions that he was the least bit interested in. So we played golf all day Monday. Tuesday morning was even lovelier and the same procedure produced the same result. There was not much debate Wednesday morning. It obviously did not make sense to go to Atlantic City for just one day. So we had five solid days of golf. On our return to Baltimore several of Dr. Howland's friends expressed their surprise at not seeing him at Atlantic City. 'Oh,' said Dr. Howland, 'thousands of doctors go to those meetings. It is quite easy to miss meeting one's friends.'

"I have the most pleasant memories of a ten-day golfing expedition on which Bill Palmer and Dochez went with us. We spent most of our time playing the Long Island courses. I recall that after a morning round at the swank National Course at Southampton, we repaired to the club house for luncheon which was a large and succulent assortment of sea food. Bill, Dochez and I assailed it with great gusto, but Dr. Howland disapproved of so much food in the middle of a golfing day—and besides the cost was $2.50. So he arranged with the affable head waiter to have just crackers and milk. We were much amused when it turned out that the price for the luncheon was fixed at $2.50 regardless of its components. This trip took place in the summer of 1915. We had such a good time that we hoped to repeat it in subsequent summers, but we never did."

Howland occasionally went duck shooting, particularly with Dr. William Sydney Thayer and once went moose hunting and shot a moose, which he regretted doing afterwards. He talked a great deal about taking up fly fishing with me and I think would have liked to have done so.

In speaking of Howland's interest in sports I ought to mention a letter which I received from him, when I was at Yale. The letter stated that he would like to come to see the Yale-Princeton football game at New Haven, if Yale were going to win, but he did not wish to come, if Yale were going to lose. Would I mind telling him if Yale would win? Yale that year had an exceedingly powerful team with a remarkable backfield. I was able to reply categorically that Yale would win and that in the second half the two Yale halfbacks, Stevens and Niedlinger, would be superior to Neale and Pond, who would play in the first half. Howland came; the final score was Yale 24, Princeton 0. Perhaps I should have mentioned this as a second triumph in diagnosis. He wrote me a letter of thanks, saying that everything had come out exactly as I said.

As perhaps surmised, one of Howland's most delightful qualities was his boyishness. One time on Halloween he asked Blackfan and me to have dinner at his house, saying that every year boys rang his doorbell and that this time he intended to catch them. He said that Blackfan could stand behind a tree at one end of the drive and I at the other and he would secrete himself in the middle. Like a prude I stayed away but Blackfan

went. The boys came and Howland caught one, who turned out to be a classmate of his son John at Gilman School. The boy remarked to John next morning, "Gee, but your father can run!"

In discussing Howland's interests in sports I should have said something regarding his physical strength. Once he had a chronic catarrhal otitis. Crowe wished to open his ear at his house, giving him a whiff of gas. I was delegated to hold him. When he began to struggle, I was totally incapable of doing it. He had a beautiful physique, like a Greek statue, and, as he grew older, retained his youthful form.

Howland was extraordinarily interested in the Civil War. He seemed to know everything about it and everything pertaining to the political situations which led to it. His father had been an officer and one of Howland's great boyhood friends was the son of General Barlow, after whom Barlow's Knoll on the battlefield of Gettysburg is named. Twice I had the privilege of visiting Gettysburg with him. He explained the contests for Culp's Hill and Little Round Top and Pickett's Charge with great vividness and pointed to the spot where the Louisiana Tigers had almost broken the northern line and, failing, been annihilated. He was able to do what no guide could do, namely, make clear the general strategy of the battle and at the same time supply all the details not found in books. The first time I visited the battlefield with him was on the occasion of the fiftieth anniversary. As we walked along Missionary Ridge, which marked the Confederate line of battle, Howland drew my attention to a Confederate veteran thrusting his outstretched fingers into the mouths of the cannon. He explained that it was the method on the field of determining the bore. On this particular occasion General Barlow's son was a member of the party. As we were walking along, I was suddenly hailed by two veterans from my home town, Gloversville, N.Y.; one was Joseph Thrall, who ran a sporting goods store and, squat and fat, was the most unwarlike figure I could have picked out and the other was a grocer named Cohen, who I should have thought would have run away at the first shot. I asked them in which regiment they had served. Both of them exclaimed, "In Barlow's Division." I promptly said, "Here is General Barlow's son. Let me introduce you," thereby rising enormously in their estimation.

It is often said that Southerners forget the Civil War is over and continue to fight its battles. But Howland felt so keenly the northern side that he would not visit the battlefield of Antietam because, as he explained, McClellan had missed *five* chances, any one of which, if taken, would have resulted not only in the defeat of Lee but in the capture of his entire army. However, I did finally succeed in enticing him to Antietam, but his sufferings were great.

Howland's sense of humor missed nothing and recorded everything and enlivened his conversation. He used to regale me with incidents which happened in connection with his Negro servants. The butler had asked for some white shirts. Dr. Howland kept, purposely or not, forgetting. Finally at a very formal dinner party the butler appeared with a short dicky and a red undershirt showing below and waited with all ceremony.

Then there was the maid who burst into his room to tell him the cook had chased her with a carving knife. Howland took off his shoes, stole down the back stairs and looked into the kitchen. There was the enormously fat cook, who in thunderstorms used to go down into the cellar and hide between the wall and the brick chimney, whetting a carving knife on her bare arm and muttering to herself, "Carve your heart

out." On another occasion the hat belonging to the maid, who was known to be light-fingered, was found in the pantry filled with eggs. When Mrs. Howland confronted her with this evidence, she explained with imperturbable innocence, "well, for the lan's sake. How do you suppose those eggs got into my hat?" There was another maid who astonished Mrs. Howland by setting out to attend the funeral of a friend wearing a bright red dress. A month later she gave notice, explaining that she was soon to be married. "You recall," she said, "that red dress I wore to the funeral? Well, that red dress caught the eye of the corpse's husband." Dr. Howland looked on his Negro servants as strange creatures, just come out of the moon, with lunar ethics and not accountable according to the rules and regulations of our society.

Howland was vastly entertained when his resident, Stewart, who succeeded Rivers, wanted to go Christmas shopping and could not find his hat, then remembered that all he had was a straw hat since he had not been out of the hospital since October.

When Ashley Weech was resident, the assistant resident was his great friend, Katharine Dodd. Howland once asked me the riddle: "What does Weech say when he gets stuck?" The answer was, "Katy, Katy, Katy." I think many of us would like to be able to cry out for Katy when in difficulties with a sick child.

One afternoon Howland came out of his office to look me up and tell me that Gamble in his first lecture to the students, which was supposed to last for an hour, had run through all his material at the end of 30 minutes and been obliged to dismiss the class.

Howland was greatly amused by Harold Higgins, who was privileged to work in the small laboratory, occupied by him and Marriott. They would call out to Higgins their mathematical problems. Higgins would look up to the ceiling in an abstracted manner for a minute or two, his mouth and tongue moving as if muttering to himself, and then would give the answer. The presence of Higgins made the solution of a mathematical problem like looking up a logarithm in a table.

Once Howland had as a guest at his home the well known Scotch pediatrician, Leonard Findlay, then of Glasgow. The two sat up arguing until two o'clock in the morning, Findlay maintaining that the essential defect in rickets lay in the calcium and Howland that it was in the phosphorus. Howland told me that he became so fatigued he didn't care what the defect in rickets was and his one thought was how to get Findlay to bed. So he said he stood up in front of Dr. Findlay and asked, "What can I do for you now?" The indomitable Scot replied, "Give me another cigar."

In contrast to his brother, Charles, who was deeply concerned by the country's social problems and used to write for the then leftist *New Republic,* even poetry, John was a staunch conservative. John, while admiring his brother immensely, I believe, looked somewhat askance at the latter's social attitudes. I have heard John remark that the working classes were getting too uppish and should be put in their places. This was in the early days of the strikes, before they had been, so to speak, legitimized. I do not think that he would have felt that way now. This does not mean that he was not extremely kind and devoted to those in his immediate environment, no matter who they were or what their circumstances, but that his social interests were fairly sharply limited to what his environment happened to include. He was not especially interested in politics and certainly not fixed in any party affiliations. Both Mrs. Howland and he, like most others of their generation, believed that children should be models of de-

portment and certainly the Howland children were such. Both Mrs. Howland and her husband accepted conventional Baltimore society and moved in the so-called "upper circles" but never to the extent of interfering with John's work which always came first. I think that Howland had little understanding of and little sympathy with psychiatry, at least as taught by Adolf Meyer. It appeared too indefinite and nebulous for his immediately practical mind. He never discussed religion with me. Dogma in any form in any aspect of life he could not tolerate. On every issue he demanded the right to think for himself. I think that speculation which seemed to him to lie outside the possibility of actual experience did not interest or trouble him. He had a high code of behavior to which he rigidly and automatically conformed and this was sufficient.

In contrast to Dr. Holt, he had little interest in and paid little attention to the child welfare movements in pediatrics and it is my impression that he looked upon the pediatricians who had made that side of pediatrics their life work as being on the whole inferior. He said to me once that he was unwilling to have his department extend into child welfare because it could not deal adequately with that and with the pediatrics of disease successfully.

In his dress and in his habits in general he was simple to the point of puritanical plainness. He wore the same felt hat for several years until it was finally lost. Mrs. Howland used to object to it loudly and I used to think got as much pleasure from objecting as he from continuing to wear it. Once, when I said to Mrs. Howland that I had the impression John did not read a great deal she emphatically contradicted me by saying that he read every evening. He went to bed about 11 o'clock. I believe that his evening reading, when I knew him, was chiefly medical, in particular the manuscripts sent in for publication to the *American Journal of Diseases of Children* of which he was an editor. But his general information was that of a wide reader of great intelligence and thoughtfulness and Mrs. Gamble has told me that on their European tour he read in advance in regard to all that they saw and knew everything beforehand. My opinion is that Howland's wide knowledge was due in large part to the excellent quality of his reading, and to his remarkable memory which held not only what he read but what he learned from conversation. He often used to quote from Lawrence Sterne. He was not particularly fond of music but liked classical music. He could quote from the librettos of Gilbert and Sullivan and also the Wagner Ring operas, the latter in the original German. When a student in Germany, he must have gone a great deal to German opera.

Howland's attitude toward money had a curious contradiction. He came to Johns Hopkins in 1912 as Professor of Pediatrics on a salary of $4,000. When the department went on full-time in 1913, his salary was increased to $10,000. When he was called to the chair of Pediatrics at Harvard University, which I think must have been in 1919, he showed me a letter written to him by Dr. Henry Christian, urging him to accept and stating that by spending not more than two to three hours a day in seeing private patients he could easily increase his income to $30,000 a year. I do not believe that Howland ever very seriously considered the Boston call, although his New England blood made him prefer Boston as a place to live. He told Graham Lusk that in Boston he could speak to anyone on a street corner and be understood. The reason he declined was that his facilities in Baltimore from every point of view were favorable for the prosecution of his work and special interests while those in Boston required de-

velopment. It would seem from this that Howland had no particular interest in money. On the other hand, he told me on two occasions that, if he were starting life all over again, he would not go into medicine at all because the remuneration was too small to enable one to live well. I remember, too, that, when I once asked him why he never bought a motor car, he replied he would not be satisfied with any car short of a Pierce-Arrow plus a chauffeur and that he could not afford. Howland had very rich friends; one was Mr. Cochrane who gave millions to Andover Academy. He could not live parallel to these friends when he was with them. He had been accustomed to wealth in his childhood. Undoubtedly there was at times a conflict. Graham Lusk reported that Howland not very long before his death said to him that the arrangement of his life was the only one suitable for his tastes and that he was perfectly happy in it. I am certain that this remark expresses the essential truth.

As a companion Howland was utterly delightful. He never controlled the conversation but let it wander naturally and seemed interested, wherever it led. His ever youthful freshness and spontaneity, his sense of fun, his power of reminiscence and mimicry, the intensity of his feelings which were always on one side or the other, never in the middle, and the wealth of his experience and knowledge gave his society an ever shifting variety and charm. But I must not forget his friendliness. He loved people and being with them and, I think, could not have gotten along in life without companionship. When with him, one could not help but be conscious of the warmth of his nature. He was one of the most companionable people I have ever known. He was wrapped up in his family and could not be happy for any length of time away from them.

What a joyous place the Harriet Lane was in those early days under this virile man! We were all young, our chief not much older than we, certainly not older in spirit, a happy family in which each had his duty. There was not a discordant soul amongst us. All was fresh, hard work was a delight and each day brought the new experiences and excitement of creative work. Then it must be remembered that this oasis of the Harriet Lane was set in the larger oasis of the Johns Hopkins, then still in its early glory, filled with interesting and some of them distinguished men, engaged in important work and having wide outlooks.

At the time of his death Howland was by far the most distinguished figure in American pediatrics and, had he lived, he would have received every honor which could have been bestowed on one of the most outstanding figures in medicine in this country. Howland was twice accorded the honor of being the lecturer before the Harvey Society of New York City. His last Harvey lecture on the "Etiology and Pathogenesis of Rickets" was a noteworthy contribution to that subject. He was a member of the Board of Scientific Directors of the Rockefeller Foundation for Medical Research, of the Council of Pharmacy and Chemistry of the American Medical Association, a director of the Russell Sage Institute and a member of numerous societies and medical organizations. In pediatrics he had become a world figure as the result of his investigative work and also his editorship with Dr. Holt of the famous textbook. In regard to his reception in Europe on his last journey, Gamble wrote me: "He was extremely happy re-visiting European clinics where he was received with admiration. Bokay met him at the door of his hospital and led him affectionately by the hand through the wards. He then assembled his students and read them a citation of Dr. Howland's contributions to which they responded with a rafter-raising Hungarian shout. We went unannounced to Feer's Clinic

in Zurich where we encountered at the door a huge intern who asked gruffly who we were. I told him meekly that he was Professor Howland from America. Whereupon the intern threw his arms in the air: 'Sind sie der berühmte Professor Howland?' How could the last two months of his life have been more appropriately spent?"

I have portrayed Howland as accurately as his Boswell has been able. He was every inch a human being and a most colorful and virile one. Dr. William Welch at the memorial exercises in his honor mentioned particularly his "sanity" and "robustness." He was a many-sided man, succeeding wherever he turned, and whatever the goal might be, he pursued it with unceasing intensity. It is often remarked that no head of a university clinical department can combine all the required qualifications, namely, an able administrator, clinician, teacher and investigator as well as leader. Howland was unique in that he did combine in rare degree each of these abilities. There was no moment in his life when he did not know success, and it is remarkable that he was not spoiled. Life was to him a great game; he loved it and played it with an exuberant vitality and always to win, and he seldom lost. I think that this drive to excel, wherever he tried, best explains his career.

If I have laughed at him, it has been the laughter of affection and admiration, such as Winston Churchill evokes. Indeed if I should compare him to anyone, it would be to Winston Churchill, in whom greatness and a freshness and simplicity of youth, a shrewdness of judgment and a naïveté are so happily and at times amusingly combined each exhibited as if the other did not exist.

I now come to the concluding question: What has been John Howland's influence? What will be his place in pediatric history? These are my impressions concerning the verdict of time: Abraham Jacobi was the pioneer. He was a man of remarkable personality, far better educated medically and culturally, when he came to this country from Austria, than his American colleagues. He had great influence in raising the level of American medicine, particularly in New York City. But in pediatrics, so far as I can tell, his merit is limited to his having been the pioneer. He was the first, I might say, officer, to wear the pediatric uniform. If he has left a permanent imprint on pediatrics, I do not know what it is.

The case of Dr. Holt is very different. Holt established pediatrics in this country as a special branch of medicine, defining it and putting it in order and he made it include the welfare of the child in health as well as in disease. It was a big revolutionary conception, the idea that the physician is also charged with keeping the child well, coming at a time when physicians in general thought that their duties began and ended with sickness. When we say that pediatrics more than any other branch of medicine is directed toward preventive medicine, we must feel grateful to Dr. Holt for having started its flow that way. John Howland modernized pediatrics. He changed the course of pediatrics to what we know it now by substituting for bedside observation and conjecture the study of disease through laboratory methods and experiments. He caused pediatrics to become a dynamic, rapidly expanding subject. He accomplished this, not by scattering ideas which caused others to act, but by example. The example lay in the development of a model clinic, model from the point of view of administration, medical care, teaching, research, spirit—the Harriet Lane Home—known all over the world and in this country extensively copied just as he left it. Moreover, he created and sent out missionaries, his pupils, filled with his ideas and spirit.

A new era in medicine, founded on the applications of science, was coming anyway. The Rockefeller Institute, for example, was founded in 1901. But Howland started the movement in pediatrics and the Harriet Lane Home under his guidance was the first full-time university clinic to win complete success. The successful experiment of the Harriet Lane insured the success of the full-time movement in American medicine.

The influence of both Holt and Howland has been in the English-speaking countries, for pediatric clinics, where disease was studied and taught on the basis of the facts found in the laboratory and by experiment, had existed in the German-speaking countries for a number of years and French medicine, until recently, has been little affected from without. But the influence of these two men in the United States and Canada has been enormous.

The contributions to medical knowledge of Alfred Hess probably rank first in importance but those of which Howland was author stand almost equally with his. They alone would have given Howland great distinction and assured him a high place in pediatric history, if they had been his sole contribution. As one of those who rose as the result of association with Howland and who benefited perhaps most from his friendship and influence, I again express my gratitude and appreciation of the award which bears his name.

NEWS AND ANNOUNCEMENTS

Dr. Myron E. Wegman, Professor and Head of the Department of Pediatrics at Louisiana State University, School of Medicine, and Pediatrician-in-Chief of the LSU at Charity Hospital of Louisiana at New Orleans, has resigned these positions to accept appointment as Director of the Division of Education and Training of the Pan American Sanitary Bureau, the Regional Office of the World Health Organization for the Americas. The responsibilities of this position will include working with the schools of medicine, schools of public health and other professional schools in the Americas connected with health activities, in order to better the general preparation of professional personnel having to do with health and medical care. Responsibility will also cover graduate training and fellowship programs sponsored by the Pan American Sanitary Bureau and the World Health Organization. It is planned that the program will develop in cooperation with other international agencies working in the field of public health and medical education. Dr. Wegman's headquarters will be at the Pan American Sanitary Bureau, 1501 New Hampshire Avenue, N.W., Washington 6, D.C. He will assume his new duties at the end of the academic year.

Dr. Nelson K. Ordway, at present Associate Professor of Pediatrics at Louisiana State University, will succeed Dr. Wegman. Dr. Ordway was graduated in medicine at Yale, interned at the New Haven Hospital and the Hospital of the University of Pennsylvania and was a member of the War Gas Research Project at Yale from 1941 to 1945. Subsequently he was an instructor in Pediatrics at Yale until he joined the faculty at Louisiana State University in 1947 as Assistant Professor, being promoted to Associate Professor in 1950. Dr. Ordway is a member of the Society for Pediatric Research and the American Pediatric Society.

* * *

The American Pediatric Society held its sixty-second annual meeting at Hotel Chamberlin, Old Point Comfort, Va., May 7, 8 and 9, 1952.

The following members were elected for officers for 1952-53: President, Dr. Irvine McQuarrie, Minneapolis; Vice President, Dr. Ernest J. Caulfield, Hartford, Conn.; Secretary-Treasurer, Dr. Aims C. McGuinness, Philadelphia; Recorder-Editor, Dr. Stewart H. Clifford, Boston; Member of the Council, Dr. Henry G. Poncher, Chicago.

The following candidates were elected to active membership in the Society: Drs. Charles Bradley, Portland, Ore.; Albert Dorfman, Chicago; Gilbert B. Forbes, Dallas; Walter Heymann, Cleveland; Robert B. Lawson, Winston-Salem, N.C.; Sherman Little, Buffalo; Donald Patterson, Vancouver; John C. Peterson, Nashville; Alan S. Ross, Montreal; Roland B. Scott, Washington; William M. Schmidt, Boston; Margaret H. D. Smith, New Orleans; William M. Wallace, Cleveland; Tyree C. Wyatt, Syracuse.

The following were elected for honorary membership in the Society: Richard W. B. Ellis, M.D., Edinburgh; Professor Sir James Spence, Newcastle-on-Tyne.

* * *

The Society for Pediatric Research held its annual meeting on May 5, 6 and 7, 1952, at Hotel Chamberlin, Old Point Comfort, Va. The following officers were elected to serve for the year 1952-53: President, Dr. Robert Ward, New York; Vice President, Dr. Milton Rapoport, Philadelphia; Secretary-Treasurer, Dr. Sidney S. Gellis, Boston. Members of the Council: Dr. Edward L. Pratt, New York; Dr. Nelson K. Ordway, New Orleans; Dr. Charles D. May, Minneapolis; Dr. Gladys J. Fashena, Dallas; Dr. Herbert C. Miller, Kansas City, Kan.; Dr. John F. McCreary, Toronto.

The following were elected to membership in the Society: Drs. Robert A. Aldrich, Portland, Ore.; Barton Childs, Baltimore; John F. Dammann, Jr., Santa Monica, Calif.; Floyd W. Denny, Jr., Minneapolis; Lloyd J. Filer, Rochester, N.Y.; Gordon E. Gibbs, Baltimore; David Gitlin, Boston; Bruce D. Graham, Ann Arbor; Robert H. High, Philadelphia; Solomon A. Kaplan, Cincinnati; Gerald Miller, Rochester; Frederick C. Moll, Seattle; Erwin Neter, Buffalo; William Obrinsky, New Orleans; James J. Quilligan, Jr., Dallas; Helen S. Reardon, Philadelphia; Andrew J. Rhodes, Toronto; Irving Schulman, New York; Roland B. Scott, Washington; Edna H. Sobel, Cincinnati.

* * *

The following candidates were certified by the American Board of Pediatrics, Inc.:

WASHINGTON, D.C.—MAY 2, 3 and 4, 1952

Adams, Frederick F., Jr., 157 Pine St., Spartanburg, S.C.
Armstrong, William Bennett, 702 First Avenue South, Fargo, N.D.
Arnold, Herbert L., Jr., 507 First National Bank Bldg., Tuscaloosa, Ala.
Baggs, Wade H., Jr., 811 Citizens Bldg., Tampa, Fla.
Baldwin, Ruth Workman, University of Maryland School of Medicine, University Hospital, Baltimore.
Blinski, Maurice, 123 S. W. 37th Ave., Miami
Bost, Roger Browning, Ochsner Clinic, Prytania & Aline Sts., New Orleans
Brandt, Ira Kive, 1535 Sunset Drive, Coral Gables, Fla.
Bruch, William M., 307 Ramsey St., Bluefield, W.Va.
Butler, Robert Elliott, 920 Winton Road, South, Rochester, N.Y.
Chasler, Nicholas Louis, Municipal Hospital, Pittsburgh
Childs, Barton, Johns Hopkins Hospital, Baltimore
Chisolm, James Julian, Jr., 4424 Underwood Road, Baltimore
Cohlan, Sidney Q., 8 Gramercy Park, New York City
Crane, Norman T., 1025 Park Ave., Plainfield, N.J.
Crawley, Eugene Harvey, 1417 W. Sixth St., Little Rock, Ark.
Dick, James, 2 Nassau Place, Hempstead, N.Y.
Dougan, Hubert Taylor, 1832 Monument Ave., Richmond, Va.
Epstein, Nathan, 5217 Lebanon Ave., Philadelphia
Eriksen, George Norton, 706 Phillips Ave., Wilmington, Del.
Finberg, Laurence, 4940 Eastern Ave., Baltimore
Frazier, Claude Albee, 806 City Bldg., Asheville, N.C.
Graub, Milton, 4623 Spruce St., Philadelphia
Greenspan, Herbert S., 4629 N. Broad St., Philadelphia
Harris, Irwin Lee, 1167 Virginia St., Far Rockaway, N.Y.
Harris, Robert Otis, III, 1514 Government St., Mobile, Ala.
Jackson, Harold Pryor, Children's Clinic, Durham Bldg., N. Main St., Anderson, S.C
Jenkins, Melvin Earl, Jr., 1829 Independence Ave., S.E., Washington, D.C.
Joseph, Clifford, 342 Main St., Torrington, Conn.
Kahn, Robert E., Harriet Lane Home, Johns Hopkins Hospital, Baltimore
Karzon, David T., 1161 York Ave., New York City
Kravis, Lillian Panzer, 44 Haverford Road, Philadelphia
Lace, Richard Edward, 208 Corbet St., Tarentum, Pa.
Lippi, Frank A., Jr., 6261 Gardenia St., Philadelphia
Luhby, Adrian Leonard, Department of Pediatrics, New York Medical College, 1 E. 105th St., New York
Lyles, Clarence C., 187 Oakland Ave., Spartanburg, S.C.
Lynch, John F., Jr., 641 N. Main St., High Point, N.C.
McGovern, John Phillip, 2202 Colston Drive, Silver Spring, Md.
McLeod, Robert N., Jr., Somerset Clinic, Somerset, Ky.
McPherson, Thomas Coatsworth, 20 Fourth St., N.W., Atlanta
Myers, Morris, 35-03 157th St., Flushing, N.Y.
Nichols, Myron McCall, University of Virginia Hospital, University Station, Charlottesville, Va.
Ogborn, Richard E., Box 2, U. S. Army Hospital, Fort Bragg, N.C.
Olshaker, Bennett, 4435 35th St., N.W., Washington, D.C.
O'Rear, Harry Barron, Medical College of Georgia, Augusta, Ga.
O'Reilly, Philip J., 257 Mamaroneck Ave., Mamaroneck, N.Y.
O'Shea, James Arthur, 11 Williams St., Andover, Mass.
Parrish, Wilmer E., Medical and Surgical Clinic, Marshall Avenue at 7th St., Longview, Tex.
Perry, Douglas Dards, 277 Main St., Bristol, Conn.
Pfeifer, Robert Thomas, Media Clinic, Media, Pa.
Potterfield, Thomas G., 1514 Kanawha Blvd. East, Charleston, W.Va.

Prentice, Stanley E., 10 Hamilton Place, Tenafly, N.J.
Rauber, Albert Paul, 153 Ridley Circle, Decatur, Ga.
Riepenhoff, John P., 2998 Sullivant Ave., Columbus, Ohio
Rosen, Sydney Irving, 548 Lawrence Ave., West, Toronto
Rosenblum, Herman, 201 Fairfax Ave., Nashville, Tenn.
Ross, Lucille, J., 801 W. End Ave., New York City
Seidel, Henry Murray, Harriet Lane Home, Johns Hopkins Hospital, Baltimore
Seiler, William C., 311 W. Washington St., Sandusky, Ohio
Skinner, Richard Green, Jr., 3241 Beach Blvd., Jacksonville, Fla.
Small, Leon I., 250 Millburn Ave., Millburn, N.J.
Smith, Alan Eugene, 2010 E. 102 St., Cleveland
Smith, Martin Henry, 118 N. Green St., Gainesville, Ga.
Steinberg, Stanley Herbert, 4214 16th St., N.W., Washington, D.C.
Tilley, John Allen, 126 Harding Road, Red Bank, N.J.
Vargas, Dharma L., Ave. Gonzalez 1106, Box 825, Rio Piedras, P.R.
Waldman, Sydney, 455 S. 48th St., Philadelphia
Walker, Lewis Harry, 513 W. Market St., Akron
Weber, John Richard, 347 W. Berry St., Fort Wayne, Ind.
Weyland, Charletta Kathern 638 Chestnut St., Lebanon, Pa.
Woodruff, Calvin Watts, Vanderbilt Hospital, Nashville, Tenn.
Young, Latimer Gorsuch, 3311 St. Paul St., Baltimore
Zupanc, Edward, Lt. (jg) MC USNR, U. S. Naval Hospital, Great Lakes, Ill.

The Board announces the following dates for oral examinations: Chicago, Oct. 24, 25 and 26, 1952.

BOOK REVIEWS

THE AMINO ACIDS AND PROTEINS, edited by David M. Greenberg, Ph.D., Springfield, Ill., Charles C Thomas, Publisher, 1951, $15.00, 950 pp.

This excellent and useful book is a worth while successor to the previous book on proteins and amino acids, edited by Carl A. Schmidt. It contains a wide range of information on chemical composition, physical and chemical characteristics of the amino acids and proteins. In addition there is considerable material on the preparation and/or isolation of these substances. There is a good chapter on the criteria of purity of protein which is useful to those interested in any investigative phase of biology. The last 4 chapters of the book (chapters 10-13 inclusive) deal with biologic and biochemical "applications" of the proteins and amino acids. Here are discussed such things as the nutritional relationships of the amino acids and the chemistry of antibiotics.

The contributors to this volume are all men of some experience and standing in their respective fields. Each chapter is outlined and has an adequate recent bibliography. The form of the book is pleasing and the diagrams and illustrations are for the most part clear.

Any active clinical or basic medical research laboratory might well have this book on its reference shelf.

A TRANSLATION OF GALEN'S HYGIENE (DE SANITATE TUENDA), Robert M. Green, with an introduction by Henry E. Sigerist, Springfield, Ill., Charles C Thomas, Publisher, 1951, $5.75, 304 pp.

It is rather unusual to present a translation of one of the first medical books of classical antiquity to the medical public of today. The history of medicine is a fascinating field, and this book is a real "mine of information" of the medical knowledge at the times of the Roman Empire. "Hygiene" is an extensive term, and beliefs and habits of that time are described throughout the book.

The introduction by Henry Sigerist and a short biography of Galen translated from Le Clerc's *Histoire de la Médecine,* give all necessary information for a good understanding of the book.

Galen's work is divided into 6 books. In the first, objectives and hypotheses of hygiene are considered. The 3 primary topics are the following: the healthy bodies; the signs occurring in them, from which diagnosis is made; and the means by which the guardianship of health is accomplished. Health itself is viewed as a sort of harmony of the various elements, according to the theories of Hippocrates. Things to be administered (as food, drink, drugs) or removed (as excrements), things to be done (as massage, walking, exercise, gymnastics) or to be applied externally (as oils) are the means by which health can be preserved.

It is assumed that a man of perfect constitution is completely free, having leisure solely for the health of his body; and while the first book shows how such a man should be brought up to the fourteenth year of age, the second book shows how his care should be extended as far as manhood. This second book is thus prolonged into the general topics of hygiene. All distinctions in form and kind of massage and exercises are enumerated; it is concluded that for the best constitution, extreme forms of massage and exercises should be avoided.

Apotherapy, bathing and how to avoid fatigue complete the subject of exercises in the third book.

In the fourth book the forms and treatment of fatigue are discussed. The ulcerous, or painful, fatigue appears following excessive exercise, or spontaneously after faulty secretion (acidity). It should be distinguished from tensive, or plethoric, and inflammatory fatigue. It can be treated by diet, catharsis and various oils.

The fifth book concerns mostly the hygiene of old age: an older age can be reached if diseases are prevented, and a proper hygiene of eating and drinking is followed.

The last book, concerning the prophylaxis of pathologic conditions, is almost a summary of Galen's medical science. Many previous books are quoted, discussing the disabilities of warm and cold disposition, anomalous body constitution, and specific morbid conditions.

The difficulties of Galen's style are overcome by the perfect translation so that reading the book is easy and pleasant. The edition is very beautiful.

BEHANDLUNG DIABETISCHER KINDER: EIN LEITFADEN FÜR DIE PRAXIS (TREATMENT OF DIABETIC CHILDREN: AN OUTLINE FOR THE MEDICAL PRACTICE), Privatdozent Dr. Karla Weisse, Stuttgart, George Thieme, 1951, 67 pp., 9 illustrations, DM. 4.90.

This brief outline summarizes the experiences of the University Children's Hospital in Frankfort, one of the best pediatric teaching centers of Germany in the after-war period. Frankfort has a diabetes tradition, since v. Noorden, whose textbook and dietetic systems were leading in Europe in the pre-insulin era, worked there. This outline contains diagnosis, treatment, prognosis and laboratory technics. Since it is written for the practitioner, emphasis is laid upon office rather than hospital problems, such as various initial signs of hypoglycemia, the indications of regular-and protamine zinc insuline and psychologic treatment. The author recommends the free diet, introduced in Germany by Stolte. This dietetic system, which renounces all restrictions and relies exclusively upon adequate insulin dosage, is a controversial problem in German medicine and certainly not accepted in our dietetic regimen. The author is convinced that most children, after being discharged from the hospital, give up their diets under the influence of family and school life and that it is therefore, better to anticipate the actual living conditions and to adjust the appropriate insulin dosage to the free diet that the child will follow sooner or later.

EDITORIAL

THE American Pediatric Society has inaugurated the John Howland Award at its recent sixty-second annual meeting in Old Point Comfort, Virginia. This Award will be made annually to an individual who has distinguished himself by his life and work as exemplifying the purposes of the Society as expressed in its constitution "to honor those who, by their contributions to pediatrics, have aided in its advancement." The Award consists of a medal bearing the likeness of Dr. Howland and a monetary award. The first Award was made to Prof. Edwards A. Park of Baltimore.

PEDIATRICS is proud to published the Address made by Dr. Park and to give importance to this inaugural. Dr. Park has chosen very properly on this occasion to tell the story of Dr. Howland as a person, a friend, and as a physician and teacher. He has thereby put on record a story of the person for whom the Award is named and has contributed to the historical value of the Award. Addresses made in the future by recipients of the Award will, no doubt, vary in their content and pattern according to the wishes of each recipient. It is to be hoped that a trend may develop to record similar stories of historical data in American pediatrics.

Dr. Park, himself, is a part of the story of American pediatrics and his position is secure for all time. It is fortunate that first hand information about Dr. Howland has been set down permanently by one who has lived with Dr. Howland and has been a part of the period. All too frequently biographies are compiled from completed material and data and there is a certain value in this necessity. But Dr. Park has told in a vivid fashion a great deal about the development of American pediatrics and has contributed first hand information about the people and personalities of those who have contributed to that development.